NORTH CAROLINA

Medical Journal

Vol. 11 No. 7
July, 1950

IN THIS ISSUE:

DIAGNOSIS OF JAUNDICE — Miller

J. O.

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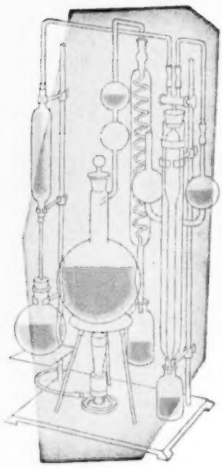

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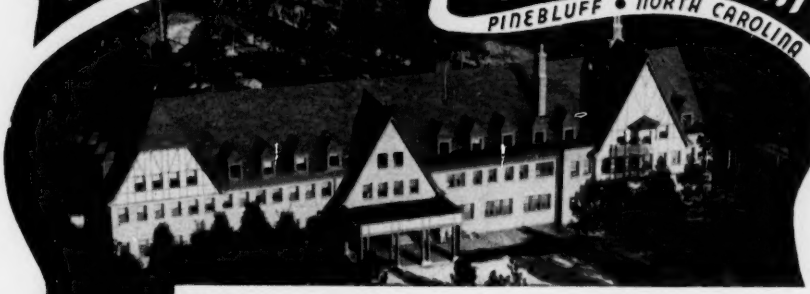

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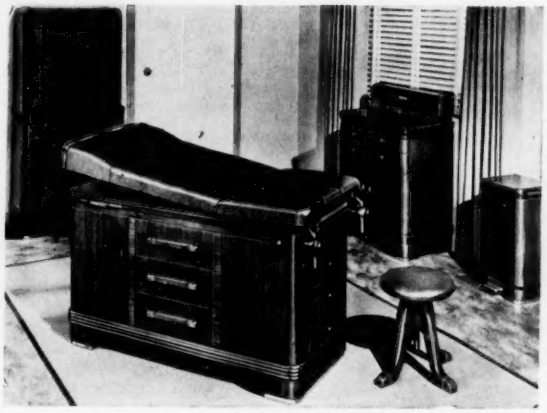

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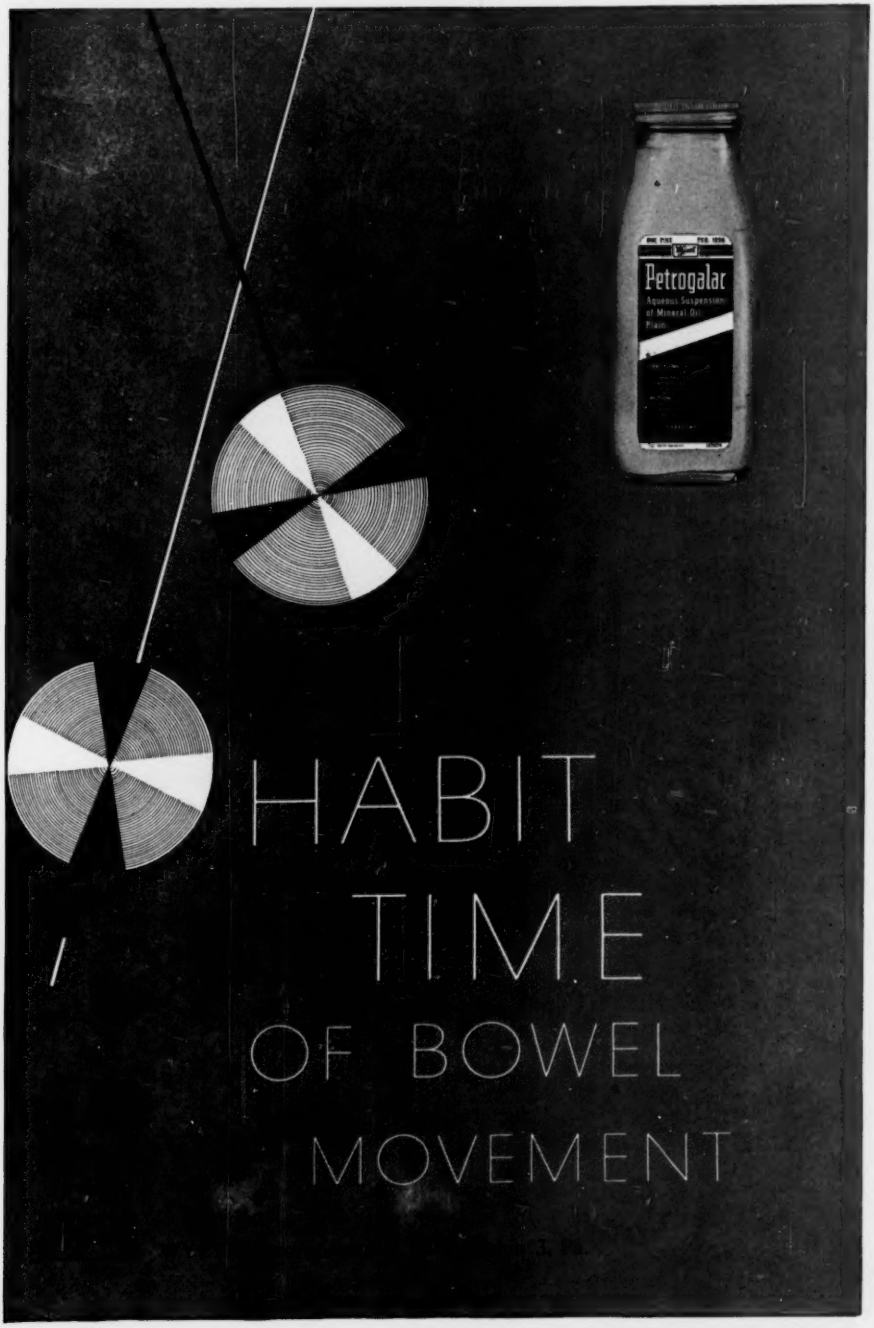
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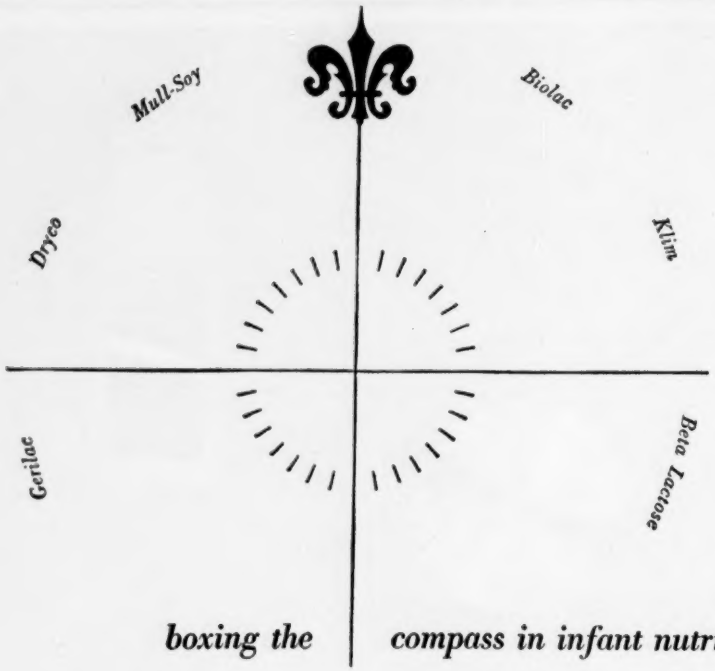

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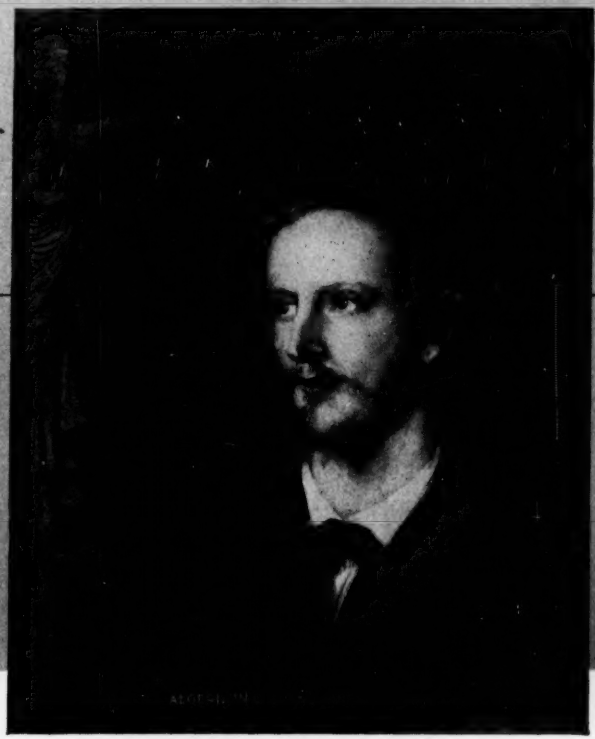

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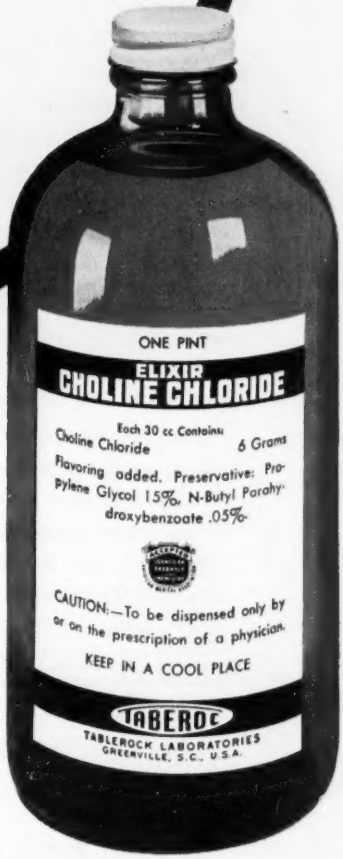
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PRACTICAL CONSIDERATIONS IN THE DIAGNOSIS OF THE JAUNDICED PATIENT

T. GRIER MILLER, M.D.

PHILADELPHIA

The word "jaundice" means yellow. By the term we ordinarily signify a yellowish discoloration of the skin that has resulted from an excess of bile pigments in the blood. In spite of that definition, we ordinarily have recognized two types of jaundice: "overt jaundice," in which there occurs a yellowish pigmentation of the skin, mucous membranes, and sclerae; and "latent jaundice," in which, although the bilirubin content of the blood is increased, it is not sufficient to cause discoloration of the body tissues. More properly the word "jaundice" should be restricted to the visibly recognizable type of hyperbilirubinemia, and the latter word should be employed to include both the overt and the latent types.

In 1939, just ten years ago, Machella and I wrote the chapter on "Diseases of the Liver" in Nelson's *System of Medicine*. In it we discussed the types and the pathogenesis of jaundice with a certain sense of finality. We classified its causes as obstructive, hemolytic, and hepato-cellular; and we unhesitatingly invoked the van den Bergh reaction in support of the classification and of the mechanisms that were described. Today that procedure for the determination of the type of jaundice has been discredited, for it has been recognized that it only confused our understanding of the physiology and of the clinical aspects of the affection.

In the meantime many new tests for the study of liver function have been developed, but they too have failed fully to clarify the problem. Although we appreciate the fact that bilirubin is derived from a breakdown of the hemoglobin of the blood and is elaborated by the reticulo-endothelial cells of the body, including those of the liver (fig. 1), we do not know the fate of that pigment. Once bilirubin has reached the liver and biliary system, we do not know with certainty how it is handled or how at times, after entering the bile ducts, it gets back into the blood stream; how sometimes it is eliminated into the urine without first having appeared in excessive quantity in the blood; or how again, though concentrated in the blood, it fails to appear in the urine. We do not fully understand the pathogenesis or associated phenomena of any type of jaundice. Consequently my subsequent statements must be regarded as largely tentative.

The Types of Jaundice

Prehepatic

What we formerly called hemolytic or retention jaundice is now, I believe, best designated, as Ducci[1] has suggested, prehepatic jaundice (table 1 and fig. 2). He recognizes two subtypes, hemolytic and non-hemolytic. Even when associated with the production of an excessive amount of bilirubin (the *hemolytic* subtype), however, prehepatic jaundice cannot be due entirely to this factor, since the liver has an enormous reserve capacity to eliminate bilirubin. Indeed, 5 per cent of that organ is said to be capable of excreting the blood's normal content of bilirubin. It has been suggested that in this hemolytic subtype of prehepatic jaundice, possibly as the result of some associated hepatic cell damage, the threshold of the liver for bilirubin excretion is raised.

From the Gastro-Intestinal Section (Kinsey-Thomas Foundation) of the Medical Clinic of the University of Pennsylvania Hospital.

Presented in the Postgraduate Medical Extension Course of the University of North Carolina at Wilmington, February 23, 1950.

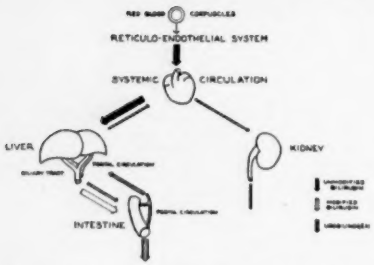

Fig. 1. The normal circulation of bilirubin, modified and unmodified, and of urobilinogen.

Table 1

Ducci's Classification of Jaundice

Prehepatic
- Hemolytic
- Nonhemolytic

Hepatic
- Hepatocellular
- Hepatocanalicular

Posthepatic
- Complete obstructive
- Incomplete obstructive

The other subtype of prehepatic jaundice, also indicated by the indirect van den Bergh test, is not at all dependent on excessive hemolysis, and so is referred to as the *nonhemolytic* subtype. It obviously is due to a raised threshold on the part of the liver for the dissociation of the bilirubin-protein complex. This type would seem to correspond to "physiological hyperbilirubinemia" as defined by Hanger[2]. He stated that this affection occurs in 2 to 3 per cent of the population, is functional in origin and may be on a familial basis. It apparently manifests itself only after emotional upsets, physical exertion, and fatigue. Neefe[3], however, in the discussion of Hanger's presentation, suggested the possibility that more intensive study, especially by biopsy and by metabolic and enzyme investigations, might eventually reveal a morphologic background in the liver.

At any rate, such non-hemolytic prehepatic jaundice may be associated, though unrecognized, with the other chief types of jaundice—the hepatic and post-hepatic varieties. The presence of only the indirect reacting bilirubin in the blood and the absence of bilirubin in the urine suggest this subtype of prehepatic jaundice, unless excessive urobilinogen in the feces, splenomegaly, anemia, increased fragility of the red cells, and other

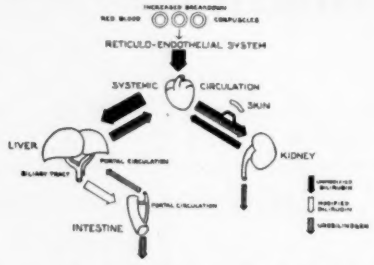

Fig. 2. Prehepatic jaundice. The formation of bilirubin is excessive. The portion modified by the liver cells has normal circulation. The remainder stays in the blood stream and reaches the skin in unmodified form; none passes through the kidney. Urobilinogen passes through the kidney in excessive amounts.

clinical phenomena support a diagnosis of the hemolytic type.

Posthepatic jaundice

Posthepatic jaundice, as defined by Ducci, is the type which was previously called obstructive or regurgitant. It may be complete or incomplete, and is characterized primarily by the presence of an excess of the promptly reacting bilirubin in the blood and by bilirubinuria (fig. 3). Hyperphosphatasemia and hypercholesterolemia also occur, and presumably result from rupture of the biliary capillaries, which permits bilirubin, alkaline phosphatase, and cholesterol — also bile salts—to be regurgitated directly into the lymphatics and the blood stream.

The bilirubinemia, however, is not always due solely to regurgitation from the biliary ducts. Once the bile pressure in the ducts reaches that of the secreting mechanism (about 300 mm. of water), no further secretion of bile takes place. Yet the jaundice, together with the bilirubinuria, persists. This phenomenon is now explained on the basis of enzyme action by the liver cells—an activity that continues even after these cells have become necrotic. Under such circumstances the posthepatic jaundice is complicated by an association of the hepatic variety. Indeed, except when associated with liver cell damage, posthepatic jaundice is not accompanied by an excessively high bilirubin content of the blood; and sometimes, when the obstruction has developed slowly and intermittently, as in common duct stone, no hyperbilirubinemia may occur.

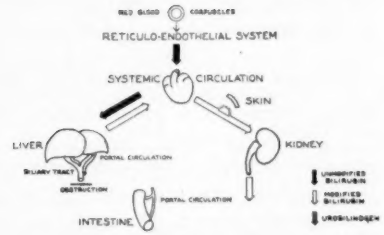

Fig. 3. Posthepatic jaundice. The bilirubin is modified in the liver and, because of obstruction, is reabsorbed. It enters the skin and passes through the kidney in modified form. No urobilinogen is formed.

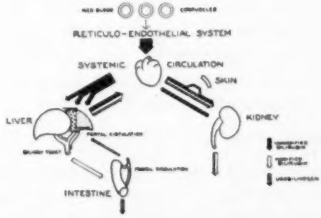

Fig. 4. Hepatic jaundice. Some bilirubin is modified and passes to the intestine; some is modified but obstructed in the small biliary radicles (small dots); some may not enter the biliary ducts because of liver cell damage (large dots) and remains in the blood stream unmodified, or this fraction may be modified by enzymes of liver cells. Urobilinogen is formed in the intestine from modified bilirubin that passes through the liver, and some of it reaches the kidney.

Hepatic or intrahepatic

The hepatic or intrahepatic type of jaundice (fig. 4), therefore, may occur secondarily in connection with the posthepatic type, and possibly also in connection with prehepatic jaundice. It also may occur independently. Presumably it may result from either functional or organic disease of the liver cells. Most often it depends on some bacterial, viral, or protozoal infection, or on some chemical agent; at times it may be due to anoxia, dietary deficiencies, or fatty infiltration. The damage may involve primarily the liver cells (the hepatocellular subtype of hepatic jaundice), or the primary lesion may occur in the biliary capillaries. Cases of the latter type Ducci classifies as the hepatocanalicular subtype, though this form presents features indicative of obstruction and previously was called intrahepatic obstructive jaundice. At any rate, in both these subtypes one finds evidence of hepatic cell damage, and usually some involvement of the biliary canaliculi.

Differential Diagnosis

Clinical findings

Fortunately it is possible in most instances to determine the cause of jaundice on the basis of clinical observations. The history alone will not infrequently establish a diagnosis of common duct stone, of hemolytic icterus, or of an infectious, homologous serum, or toxic hepatitis. A long story of indigestion, finally leading to colicky attacks unrelated to meals and sometimes occurring in the night, especially in a woman having had one or more pregnancies, clearly indicates gall stones. Sometimes a similar history, but with less severe attacks of pain and more impairment of general health, is related by the patient with a malignant pancreatic lesion.

Detailed physical examination frequently yields convincing evidence of the nature of the jaundice. This is especially true for the hemolytic type, in which pallor and splenomegaly are demonstrable, and in which studies of the blood and feces usually give the final answer. An enlarged, firm, and irregular liver may at once suggest malignant disease. Metastatic nodules may also be palpated. In severe and long standing liver disease, spider nevi may accompany the jaundice and leave little doubt as to the presence of intrahepatic anatomic changes.

When the jaundice appears in a young person and is associated with fever and vague digestive symptoms, especially in the midst of an epidemic, and when there is slight hepatic enlargement and tenderness, infectious hepatitis is almost certain. If the jaundice occurs within four to six months after the subcutaneous or intravenous administration of some blood product, if it comes on insidiously and if the patient is afebrile, one suspects homologous serum jaundice. In all such cases, however, the simpler laboratory procedures are indicated, even if only for confirmation of the diagnosis.

In other instances, when jaundice appears without suggestive symptoms or signs, entire dependence must be placed on special investigations, including at times liver biopsy and even abdominal exploration. In such cases the physician must determine first of all

whether or not operative therapy is indicated. This problem resolves itself largely into a decision as to whether the causative disturbance is hepatic or posthepatic—whether it is hepatocellular or due to extrahepatic biliary obstruction.

The significance of urobilinogen studies

Because of its value in differentiating the types of jaundice, I shall now refer to the origin and fate of urobilinogen. This pigment is formed in the colon as a reduction product of bilirubin. For its production bile must reach the intestine. Of the total amount produced in the bowel, according to Watson[4], one half normally is lost in the feces, the other half being absorbed. Most of the absorbed portion is disposed of in some unknown way, probably by the liver, though a slight portion passes on from the portal into the general circulation and is eliminated by the kidney. Another small amount is passed through the liver back into the intestine.

When the liver cells are damaged, they cannot dispose of the urobilinogen reaching them through the portal circulation; then a larger quantity reaches the general circulation and is excreted by the kidneys. Consequently, when the urobilinogen of the urine is excessive in amount, we know that bile is reaching the bowel and, if hemolytic jaundice and partial biliary obstruction are ruled out, that the liver cells are damaged. Hyperbilirubinuria occurs, for instance, in viral hepatitis and in other diseases affecting the liver cells.

When hemolytic or retention jaundice is present, the differentiation may be made, in addition to the clinical and hematologic observations, on the basis of a very marked increase in the urobilinogen content of the feces together with acholuria. On the other hand, in complete obstruction, as from carcinoma of the head of the pancreas, little or no urobilinogen is found in the duodenal contents, the feces, or the urine. If, however, the obstruction is incomplete, as is usual in common duct stone, the feces are bile-stained, and urobilinogenuria, as well as bilirubinuria, is found. It must be pointed out that in some instances of severe viral hepatitis and of toxic hepatopathies, no bile passes into the bowel and, under such circumstances, no urobilinogenuria occurs, just as in complete obstruction.

Table 2
Usual Laboratory Results in Uncomplicated Types of Jaundice*

Chief Types		Pre-Hepatic	Post-Hepatic	Hepatic
Serum bilirubin	Prompt(1')	N	I	I
	Total	I	I	I
Urine bilirubin		O	+	+
Urine urobilinogen		I	O or N	I
Feces urobilinogen		I	O or D	N or D
Ceph. chol. floc. and thymol tests		—	—	+
Alkaline phosphatase		N	I	N
Cholesterol	Total	N	I	N or D
	Esterified	N	N	D
Prothrombin response		N	N	D

N = normal I = increased
D = decreased — = negative
+ = positive O = absent
*Some of the variations are referred to in the text.

Other special tests

In the differentiation of hepatic from posthepatic jaundice other special tests are available (table 2). The former produces disturbances in the serum albumin and globulin, as indicated by a positive cephalin cholesterol flocculation test and by positive thymol flocculation and turbidity tests. These are absent in the uncomplicated obstructive or posthepatic type. In the latter, however, the alkaline phosphatase and the cholesterol values of the blood are increased.

While these various tests are clearly indicated in all obscure cases of jaundice, they must not be depended on exclusively. Confusion can arise from the fact that, as has been indicated, the various types of jaundice are frequently associated and also from the fact that the particular hepatic structures involved in any one disease may vary. Thus in infectious hepatitis the involvement may be limited to certain parts of the liver: the parenchyma, the Kupffer system, or the perilobular spaces. Unless the hepatic cells are involved, the flocculation tests usually are negative. Hepatic jaundice also may occur on the basis of passive congestion or of a liver tumor, when the flocculation tests may be negative. In addition, the tests themselves are not pathognomonic. Even an increase in the blood alkaline phosphatase may result from certain bone diseases or from a hepatic neoplasm, as well as from biliary obstruction.

If the lesion is extrahepatic, the blood will contain an excess of promptly reacting bilirubin and of alkaline phosphatase. The urine

under such circumstances will contain bilirubin, and, unless the obstruction is complete, also some urobilinogen. If the obstruction is complete, no urobilinogen will appear in the duodenal contents, the feces, or the urine. The cephalin cholesterol flocculation and the thymol turbidity tests will usually be negative unless secondary damage to the hepatic cells has developed. In an advanced case of complete obstruction, as from carcinoma of the pancreas, no bile will appear in the feces, while in a case of common duct stone some usually does occur from time to time. It must be remembered, however, that sometimes, even without obstruction, the stools may be acholic. In that event the flocculation tests usually are positive.

For the differentiation of obstructive and nonobstructive jaundice, both giving acholia, a determination of the prothrombin time of the blood may be very helpful. If the prothrombin concentration in the blood is low and the liver cells are intact, the administration of synthetic vitamin K will promptly bring about a return of the prothrombin to normal. In the presence of excessive hepatic cell damage, however, no such effect can be obtained.

A picture suggestive of posthepatic jaundice may result from hepatic disease which involves only or mainly the cholangioles. As has already been stated, this condition was formerly referred to as intrahepatic obstruction. In early stages of this affection, as in posthepatic jaundice, the liver function tests, except for hyperbilirubinemia, are negative. This picture occurs in cholangitis, in toxic degeneration and tumor of the liver, and, according to Ducci, after the therapeutic use of arsenic, the sulfonamides, or thiouracil, and sometimes after viral hepatitis. In some cases liver biopsy may be required to make the diagnosis; in others surgical exploration of the abdomen may be the only means of finally settling the matter. When at such an operation no extrahepatic lesion is found, clinical experience suggests that it still may be justifiable to drain the gallbladder. Not infrequently this procedure brings about relief.

Intrahepatic disease should be suspected in all jaundiced patients in whom no convincing evidence of either prehepatic or posthepatic jaundice is found. It should be regarded as probable when the cephalin flocculation and thymol turbidity tests are positive. It should be suspected in association with prehepatic jaundice when there is a considerable increase in the promptly reacting bilirubin of the blood and bilirubinuria as well as positive flocculation and turbidity tests. In patients with posthepatic jaundice it should be suspected when, in addition to the symptoms, signs and laboratory evidence of biliary obstruction, the bilirubinemia is very marked, and the albumin, prothrombin, and cholesterol ester values are reduced.

Many variations, not as yet explainable, occur. In the early stages of infectious hepatitis, for instance, before hyperbilirubinemia occurs, bilirubin and urobilinogen may be found in the urine; and, later in the convalescent stage, when the pigments have disappeared from the urine, some elevation of the bilirubin of the blood may still be demonstrable. This finding suggests some alteration in the permeability of the renal glomerulus for bilirubin and urobilinogen—a factor that has not as yet been elucidated, but one that may influence the concentration of these pigments in the blood and urine under other circumstances.

Conclusion

No attempt has been made in this presentation to cover exhaustively the subject of jaundice, or even to mention all of the clinical and laboratory procedures available for its investigation. Instead, I have merely tried to outline, on the basis of a recently proposed classification, some of the more simple methods now available by which the various types can usually be recognized.

The figures were prepared by Dr. Mary Lou Haanes, whose assistance is gratefully acknowledged.

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THE CHANGING EMPHASIS IN COMMUNICABLE DISEASE CONTROL

CECIL G. SHEPS, M.D., M.P.H.

CHAPEL HILL

Recent changes in the control of chronic communicable diseases such as tuberculosis and syphilis are frequently discussed. It appears, however, that there is a tendency to take for granted our programs for the control of acute infections, in spite of the important changes in emphasis which are taking place. It is, therefore, largely toward these latter problems that these remarks are directed.

Governmental responsibility in the control of communicable diseases has long been recognized. The modern public health movement is barely one hundred years old, and it is interesting to note that for the first sixty years—that is, until the beginning of the personal hygiene movement around 1910—the control of communicable disease was the sole *raison d'etre* of health departments. This function has been carried out largely by the application of three basic procedures: isolation and quarantine, environmental sanitation, and immunization.

As scientific knowledge accumulated, our notions as to the relative value of these procedures have been modified, as has the emphasis we have placed on each in specific control programs.

The efforts of organized public health activities have been largely responsible for removing "from modern life the treacheries of many diseases which once menaced the development of our urban civilization." This, the oldest function of preventive medicine, is full of triumphs. If you could say to an individual patient, lying on his death bed, "I will give you twenty-five more years of life," it would be recognized as a miracle. And yet, that is precisely what has been accomplished in four generations. In 1850 the expectation of life at birth in this country was only about forty years. Today it has risen to sixty-seven years. Most of these gains in the expectation of life have been made in the population under the age of 50, and are due mainly to the control of communicable diseases. Between 1900 and 1920 the reduction in the incidence of typhoid, tuberculosis, diphtheria, diarrhea, and enteritis alone corresponded to a saving of 230,000 lives each year in the United States.

"Public Health has a future as well as a present and a past." As a result of its triumphs, we now have a population with an increasing proportion of older people. An evaluation of present day health problems brings to the fore the need for more emphasis in new and challenging fields of public health activity. Dr. Winslow has recently said, "The health officer who is interested merely in back yards and quarantine signs dates back to 1900. The health officer who adds to this immunization, child welfare and tuberculosis clinics dates back to 1930."[1] On all sides we are being adjured to introduce or extend such programs as cancer control, dental hygiene, diabetes, cardiac disease control, mental hygiene, accident control, and multiphasic screening.

In the face of these necessary developments, what is to be done about our time-honored responsibility and procedures for the control of communicable disease? Do we simply graft these new programs on to the old ones? Or is our job done in communicable disease, and can we therefore let it slide into neglect?

It is clear that our job in communicable disease control is not finished. We still have people dying of completely preventable communicable diseases such as diphtheria. The recent outbreaks of smallpox in New York City and on the West Coast are also cases in point. If we think beyond deaths and consider sickness and disability caused by infectious conditions, it is apparent that there is still much to be done. In addition to unfinished work which remains to be done in the control of some of the infections which have traditionally occupied health departments, there are new problems confronting us as a result of recent scientific developments.

Basic Procedures in the Control of Communicable Diseases

Quarantine

We realize now that the abounding faith which we all had in the effectiveness of quarantine is not justified. Until fairly recently, disinfection by fumigation was believed to be the answer to the prevention of

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infectious disease. Even as late as 1898, the notion that disease was due to the gaseous products of decomposition, and particularly to the deadly nature of sewer gas, was so widely held that G. A. Waring was sent to Havana to stamp out yellow fever by cleansing the city. His efforts resulted in making Havana one of the cleanest cities of its time —but the yellow fever continued[2].

The science of bacteriology gave us the information that the control of communicable disease involves the control of contagion. Therefore we began to direct our attention more to groups of persons and to individuals. The notion that the strict isolation of infected persons and the quarantine of their contacts would stamp out disease has long since been shown to be wrong. And yet, when we examine the regulations under which many health departments operate, it is obvious that the limitations and inherent deficiencies of these restrictive measures are not yet sufficiently appreciated.

Some of the more important deficiencies of these restrictive measures are:

1. Most cases of the communicable diseases are highly infectious before they become recognized clinically.

2. The plan presupposes that every case of the disease is readily recognized. This is seldom true.

3. The health department is seldom notified of all the cases which are diagnosed.

4. Healthy carriers are often hard to detect.

5. These measures constitute a great interference with personal liberty. They often may mean a serious loss of earning power or a considerable loss of time from school.

Between 1910, when Dr. Baker began her work in the New York City schools, and the second World War, when extensive experience was obtained in army camps, sufficient evidence has accumulated to show that, rather than enforce a rigid quarantine of all contacts, it is much more efficient from all points of view to let contacts proceed with their activities as long as they are carefully examined each day during the incubation period. Certainly these are procedures which are practical in our city health departments.

The recommendation regarding placarding made by the American Public Health Association, the Public Health Service, and the United States Army and Navy and Air Force reads in part as follows[3]:

> "Placarding, as practiced in the United States, does not aid significantly the efforts of a health department to control acute communicable diseases ordinarily spread directly from person to person in the United States (chickenpox, mumps, pertussis, measles, diphtheria, scarlet fever, anterior poliomyelitis, meningococcus meningitis, pneumonia, tuberculosis, gonorrhea, syphilis); consequently it is not recommended for these diseases.
>
> "Placarding has definite disadvantages: it is difficult to enforce, it may be a deterrent to reporting, it is costly in transportation. The most serious objection is the loss of time of public health nurses and other health department employees which should be devoted to practical instruction in the observance of isolation and concurrent disinfection at the bedside of patients suffering from the more serious communicable diseases."

In North Carolina, placarding is still mandatory for five of the diseases listed, and optional for three.

Uniformity of procedure is not a virtue in itself. It does seem desirable, however, that our administrative regulations should be in agreement with the scientific facts which are relevant to each situation.

Another example of our undue emphasis on restrictive procedures is the hospitalization of patients with communicable disease. The arrangements and facilities presently available are uneconomic and ineffective. We have progressed from the era of the pest houses to that of isolation hospitals which, according to the 1948 American Medical Association Directory of Hospitals, had an average occupancy rate of only 43.6 per cent. Students of this problem have recently suggested that special facilities and proper techniques be established as an integral part of general hospitals. "These can be readily provided and made available for use when the occasion demands this specialized service. However, during periods when little communicable disease is prevalent in the community, these same accommodations could be used for patients with non-communicable acute illness, thus providing a flexible service to meet the needs of the community."[4]

This plan is of special value in rural areas, because the expansion of such a service in the community hospital would make possible more complete care to residents in the area, and would provide a ready means for isolating cases of an illness which otherwise might develop into epidemic proportions. Such an arrangement bespeaks the appointment of the local health officer as an active staff member of the hospitals in his jurisdiction, and facilitates his becoming the consultant to the private physicians in the management of their cases of communicable disease. Such a relationship can be expected to be of real value in bringing about a better understanding of the health department on the part of the practicing physicians, with attendant benefits to all aspects of the public health program.

Environmental sanitation

In an effort to draw attention to some of the newer problems in public health today, statements are often made which lead one to believe that the job of environmental sanitation has been completed—that the environment of Americans is both safe and static. As Dr. Wolman says, these statements "would lead one to believe that the role of the (sanitary) engineer in modern society is primarily one of a resurrected mummy, graciously invited to review the history of a dead function. . . . How sound is the concept that the United States has passed through the period of necessary environmental control with such success, assurance and probability of continued safety that its guardians of health may climb on the next band wagon in public health activity while simultaneously discharging the baggage of the 'Golden Age of Sanitation'?"[5] If our vigilance is slackened, the great achievements which resulted from previous sanitary efforts will quickly be lost. Environmental sanitation has not yet reached the maximum limit of its effectiveness. Its charter in the public health program needs to be extended and not curtailed.

It behooves us, however, to reconsider some aspects of this program. It should be made more positive and creative, rather than corrective, and should concentrate on those procedures for which there is a sound scientific basis. Sanitary control of our sewage wastes is not yet an accomplished fact. In the five years of new housing construction in the United States ending in 1947, more cesspools and privies were added than the health officers and engineers removed in the previous twenty-five years[5]. These are some of the matters which deserve our attention, even at the sacrifice of preoccupation with nuisance complaints, dead horses, chicken houses, and ash piles. Environmental sanitation is the Gibraltar upon which is based our protection from epidemics of intestinal disease.

Immunization

The third weapon in the control of communicable diseases is the technique of specific active immunization. Here we have a potent factor indeed to insert into the eternal conflict between the population and the infectious agent. Active immunization has very drastically reduced the incidence of diseases such as diphtheria. In the past, however, the immunity produced by artificial exposure to an antigen was intermittently reinforced by subclinical exposures to the disease itself. As the incidence of cases has decreased, the number of such exposures has also decreased, with a resultant reduction in the opportunity for "latent immunization." This function must therefore be performed by reinforcing or "booster" doses given at suitable intervals —a procedure which becomes increasingly necessary.

In 1935, the American Public Health Association recommended that all children should be actively immunized against diphtheria at 6 months without prior Schick testing. In 1936, a standard pediatrics text had this to say in the chapter on diphtheria: "By the injection of toxin-antitoxin mixtures, it is possible to confer a lasting immunity on from 70 to 90% of all children so treated."[6] In 1945 the American Public Health Association recommended that toxoid be given at 6 months, with a *reinforcing* dose on entrance to school. Today's American Public Health Association recommendation is that toxoid be given by 6 months, and that "if diphtheria is to be more effectively controlled, the giving of reinforcing doses in preschool life, on entrance to school, and throughout school life and early adulthood must be considered."[7]

A recent epidemic of diphtheria in New York State is a case in point.[8] In a small township with a population of about 1200 there were reported, last December, 11 cases

and 2 deaths in a ten-day period. For the last two years, this area has been considered well immunized against diphtheria, because 72 per cent of the children under 5 years of age were known to have received a series of two doses of diphtheria toxoid. It appears, however, that few children in the area have ever been given a reinforcing dose of toxoid.

This necessity for seeing that a population is compensated for being rendered "epidemiologically innocent" also applies in tetanus, pertussis and smallpox.

Typhoid Control

The problem of typhoid control provides an excellent exercise in evaluating the role of the three basic procedures employed. The use of quarantine should clearly be restricted to carriers and to family contacts who are food handlers. The most effective means of protecting the public against typhoid is, of course, sanitation. In the early part of this century the practicing physician saw many more cases of typhoid fever than obstetrical cases. In 1900 more than 23,000 people in the United States died of this disease. In 1947 there were only 282 such deaths. There can be no doubt that this miracle is due chiefly to the sanitary control of the products of defecation and to the purification of our water supply.

What is the role of typhoid vaccination today? Its value in lowering the secondary attack rate is established. The need to use it for the protection of groups of people who are subject to unusual exposure by reason of occupation or travel is unquestioned, as is its value to those for whom immunization can be systematically and economically applied, as in military forces and institutional populations. With the present incidence of typhoid in this country, approximately 50,000 persons would have to be vaccinated, and given booster shots every year or so to prevent one case. In 1948 there were 62 cases of typhoid in North Carolina[9]. This would mean immunizing more than 60,000 persons to prevent a single case. How much better it would be to concentrate on getting adequate coverage with diphtheria immunization—for there were in the same year 509 cases of that disease reported in North Carolina[9]. The case fatality rate of both diseases is roughly the same.

It would appear that much of the health department's money and time spent on typhoid vaccination could be directed with greater effect into other channels. If we maintain and strengthen our sanitary defenses, the dwindling problem of typhoid control is largely one of the discovery and control of carriers—a fact which ought to be faced. In these times of shortage of funds and personnel, there can be little justification for a continuing program of mass typhoid vaccination except in areas of high endemic incidence — a category in which North Carolina does not at present belong.

The Role of Natural Resistance

It has long been recognized that there is such a phenomenon as natural resistance to infectious disease—and that this is of a nonspecific character. Evidence in support of this belief is found in the British and Canadian studies of the measles and whooping cough mortality rates[10]. These declined markedly in the years between 1920 and 1940. This decline was due to a decrease in case fatality rates rather than in incidence, and there was no difference in the age distribution of cases.

This simultaneous and equal decline in the case fatality rates of these two communicable diseases cannot be attributed to the introduction of any specific or otherwise effectual therapeutic measure, or to parallel reduction in the virulence of the micro-organisms involved in the two diseases. It is suggested that these declines are due to a common factor affecting the diseases similarly. What comes to mind, of course, is the gradual improvement that took place during that time in the general physical and social welfare of children, as evidenced by the virtual disappearance of the previously common marantic, sub-standard, debilitated child. There is also experimental evidence from the clinic and the laboratory indicating that the food we eat affects our resistance to infectious disease[11].

The Importance of "Minor" Infectious Diseases

A re-evaluation of our attitudes toward the so-called "minor" infectious diseases of childhood has become mandatory since the brilliant demonstration in 1941 that German measles occurring in the first four months of pregnancy causes congenital defects such as deafness, cataracts, and heart disease in

more than 50 per cent of the infants[12]. This finding raises the question as to whether young girls should be deliberately exposed to rubella.

Relationship of Communicable Diseases to Cardiac Problems

The increasing interest in the application of public health methods to the control of cardiovascular diseases has brought out some important inter-relationships between the control of communicable diseases and cardiac problems. The relationship between rubella and congenital heart disease has been mentioned. Diphtheritic heart disease can, of course, be completely prevented. The prevention, adequate treatment, and follow-up of cases of syphilis will eventually lead to the elimination of heart disease of syphilitic origin. Recent evidence concerning the relationship of hemolytic streptococcal infection to rheumatic fever points to the importance of applying all known techniques for controlling its spread and preventing its effects[13]. The role of the carrier has been shown to be important. Emphasis must be placed on the early treatment of all streptococcal infections with penicillin to prevent attacks of acute rheumatic fever, and on sulfonamide and penicillin prophylaxis to prevent recurrences among patients who have had rheumatic fever.

Summary

At this moment in the development of public health, when programs are extending into many new and important fields, an evaluation of our time-honored programs for the control of communicable disease indicates, not only that they can not be neglected, but that they have not yet reached maximum effectiveness. The established programs of the past need to be re-evaluated in terms of their present effectiveness. This re-evaluation involves developing new techniques and strengthening those procedures which are useful, as well as discarding those which are no longer of value.

A fuller recognition of the limitations and inherent deficiencies of quarantine and isolation needs to be translated into our manuals of procedure. Environmental sanitation must be given the opportunity to complete its job and thus, among other things, protect us from infectious disease of intestinal origin. Active immunization must be provided, as often as necessary, in order to maintain a protective level of immunity in a population which has diminishing opportunities to benefit from subclinical exposure.

Recent light on some of the factors involved in producing general resistance to infections strengthens our interest in nutrition and in broad health and social measures. The information presently available on the cardiovascular diseases which are preventable shows that communicable disease control is not a distinct, separate and isolated activity, but that it is intimately related to many other areas of public health interest and responsibility.

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The heritage of science. The open mind, the reliance on example and persuasion, rather than on authority—these are the heritage of the centuries in which science has altered the face of the earth. Science can help in diverse ways in preserving and extending this heritage. Its very universality speaks across frontiers to make truth manifest in lands otherwise darkened; its material applications create the preconditions—in leisure, in education, in means of communication—for the converse of men with each other. Science provides the material and the intellectual basis for a world in which example and understanding can help all men to fulfill their hopes. Today we need to remember that our country, founded on these practices, and grown strong by their exercise, owes its strength to them. In this time of crisis, we need to cherish that strength.—Openheimer, Robert: Encouragement of Science, Science 111:375 (April 4) 1950.

"ANTABUSE" IN THE TREATMENT OF CHRONIC ALCOHOLISM

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The first publication on tetraethylthiuram-disulphide (trade name, "Antabuse") and its effects in sensitizing the organism to alcohol appeared in December, 1948[1], and the result of therapeutic trials was reported at the same time[2]. In this country, as in Europe, work with this drug is going on in many centers, but published results are few. Our purpose in presenting this paper is to evaluate the results obtained in a series of chronic alcoholic patients treated with Antabuse† during the past year.

Routine of Therapy

Hospitalized patients

A routine of therapy for hospitalized patients has been evolved which, in our experience, has proved to be most satisfactory. Patients are hospitalized for a period of four to six weeks. It was requested that all patients be sober at the time of admission and that they come asking for treatment, "of their own free will and accord." In spite of this request 30 per cent were inebriated upon arrival at the hospital.

Immediately upon admission, the routine of the hospital and its rules and regulations were explained to the patient, and he was shown to his room while a complete medical, developmental, and psychiatric history was secured from members of the family. The patient was given a thorough physical and neurologic examination, and blood and urine were secured for routine laboratory studies. If the patient was intoxicated at the time of admission, he was given an intravenous injection consisting of Coramine (2 cc.), vitamin B complex (2 cc. of a soluble preparation), regular insulin (20 units), and a 50 per cent solution of glucose (44 cc.). This usually had an adequate "sedative" effect and aided in the sobering up process. Occasionally the same mixture was repeated one hour later; rarely was it necessary to use other forms of sedation. If the patient was admitted in a typical post-alcoholic state, with headache, tremors, and agitation, he was given 30 mg. of Pyrahexyl, a synthetic marihuana-like derivative, three times daily for two days.*

Following the admission procedure and initial examinations, the patient was given a psychiatric examination and a battery of psychologic tests designed to examine all of his personality and intellectual spheres. This battery consisted of a complete Wechsler-Bellevue intelligence test, a Rorschach test, a graphic Rorschach test, and a Grassi block substitution test. This last test was designed primarily to test abstract and concrete intellectual functions, to determine whether these had been impaired. When indicated, other tests of organic brain damage, as well as the Thematic Apperception test, were given. The purpose of all the tests was to enable the psychiatrist in charge of the case to understand the patient better as a functioning personality rather than "just another alcoholic."

Following these examinations, insulin subshock therapy was begun and was continued for about three weeks—the exact length of time varying with the patient's need for this type of therapy and his response to it. This treatment was given in the mornings before breakfast, and was followed by "brunch" at 11 a.m. In the afternoons, the patient's time was filled with occupational and recreational therapy, physiotherapy, and swimming. During the afternoons the patients were also seen in psychotherapeutic sessions by the psychiatrist. At some point during the first few days of his hospitalization, each patient was asked to write a complete autobiography. This was evolved in order that the patient could put down and examine in a logical sequence all of his past experiences in the light of his present situation.

During the second week of hospitalization the patients were given a bromsulfalein liver

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*A report on this will be published later by the authors.

function test. Any patient showing more than 15 per cent dye retention at forty-five minutes was rejected for Antabuse therapy, as this degree of retention was considered to be definite evidence of hepatic dysfunction. Any patient showing moderately severe cardiovascular disease was also rejected. The number rejected for these reasons was gratifyingly few. In this initial series no patient was rejected for psychiatric reasons.

Toward the end of the course of insulin therapy, Antabuse was started in doses of 1 Gm. daily at bedtime for a total of four days. On the fifth morning, before breakfast, a test dose of alcohol was given to determine the degree of sensitivity achieved. After the patient's blood pressure and pulse had been charted, he was given one third of an ounce of 90 proof whisky. Following the ingestion of the whisky, his blood pressure and pulse were recorded every five minutes, and notes were made as to his facial coloration and subjective complaints. The dose of whisky was repeated every thirty minutes until a satisfactory reaction was obtained. This was evidenced by moderately severe facial flushing, conjunctival injection, an increase of 30 points or more above the resting pulse rate, a decrease of 20 points or more below the resting systolic blood pressure, and subjective complaints of tightness in the chest, headache, nausea, and a general feeling of being "unwell." If the patient desired another drink after the reaction occurred, he was given one.

After the initial test with alcohol, the dosage of Antabuse was regulated according to the severity of the reaction and the amount of whisky required to bring about the desired reaction. In most patients it was reduced to 0.5 Gm. daily, and the test dose of alcohol was repeated after another four days. The optimal reaction should occur, in a sensitized patient, in less than five minutes after the ingestion of one third of an ounce of whisky. This reaction time will prevent a patient from finishing his first drink, much less starting a second drink. When this degree of sensitivity is achieved, most patients are continued on a maintenance dosage of 0.25 Gm. of Antabuse daily.

The drug is given at bedtime because about 25 per cent of our patients complained of lethargy and drowsiness following the original dose of 1 Gm. We also feel that it is advisable for patients to establish a habit of taking the drug at bedtime along with their evening "toilette," when it will be easier for them to remember it, and when its mildly sedative action is desirable.

Occasionally a patient has a severe reaction to alcohol which necessitates termination of the test. This can be accomplished by allowing the patient to inhale oxygen for a few minutes, or by the intravenous administration of 1000 mg. of vitamin C. The latter technique will bring about recovery for about fifteen to thirty minutes, and then the patient may have a relapse. The oral administration of 1000 mg. of vitamin C simultaneously with the intravenous injection forestalls the relapse. It has been reported that 5 cc. of a 10 per cent solution of sodium thiosulfate given intravenously will also terminate a reaction[3], but we have had no experience with this drug.

When he is discharged from the hospital, the patient is given an appointment to return for a follow-up examination, psychotherapy, re-testing, and a regulation of dosage if this is indicated. He is given a sufficient amount of Antabuse to last until his return, at which time a new supply is issued. He is also given a card to carry, bearing his name, address, telephone number, and the name and telephone number of Graylyn. It also contains a description of the reaction which will occur if the patient ingests alcohol.

Following discharge from the hospital, patients are seen every three to four weeks on an outpatient basis until the therapy is completed.

Outpatients

In the case of those treated as outpatients from the start, a similar work-up, including the physical, psychiatric and psychometric examinations and the autobiographical sketch, is used. Studies of the urine, blood, and liver function are made. Antabuse is then begun without a period of physical and psychotherapeutic rehabilitation, and the patients return for re-tests and psychotherapy at gradually increasing intervals.

Results

Thirty-six of the patients in this series were admitted to Graylyn, and 22 were treated as outpatients. They have been followed for periods varying from three to eleven months.

Hospitalized patients

Eleven of these patients have been followed from three to six months, and 23 from six to eleven months. We have lost track of 2 patients, but it is known that they have ceased taking Antabuse. Table 1 shows the results obtained in hospitalized patients, as determined by follow-up studies.

Table 1
Results in Hospitalized Patients

	6-11 months	3-6 months	Totals
Still on Antabuse	18	9	27
Stopped drug of own accord	4	2	6
Died	1	0	1

The 27 patients who have kept to their treatment have remained sober, though one patient reported a single episode of drinking when he ran out of Antabuse. Of the 9 remaining, 4 continued on Antabuse for less than two months (the 2 patients who were not followed are included in this group, although they are not listed in the table), and 5 stayed on the drug six months. Of these 5, one died of coronary disease, one has returned to renew treatment, and another is reported as sober, although not taking Antabuse.

We may therefore claim satisfactory results in 30 out of 36 hospitalized patients—a failure rate of only 16 per cent.

Twenty-nine of these patients were continuous drinkers; 7 were sporadic "spreers." Pathologic indulgence in alcohol had been known to exist for periods ranging from six months to fifteen years, the average being 5.3 years. Our group is not large enough to permit valid conclusions, but it appears that the length of history has little bearing on the results of treatment with Antabuse. Previous treatment had been obtained by 31 patients. Thirteen had been committed to an institution; 11 had had more than one voluntary admission to a hospital; and 7 had had psychiatric care as outpatients, or only one hospital admission. Only 5 patients denied having had previous treatment. We feel that the results obtained with Antabuse are more impressive in view of this high incidence of failures with previous treatment.

Outpatients

Of the 22 patients in this group, 15 were patients who volunteered for treatment after a lecture to Alcoholics Anonymous. They were treated free. We felt that the prognosis in this group, which was unselected by us except in regard to their physical condition, was extremely poor. Of 60 attending the lecture, 40 volunteered for treatment, and only 15 arrived. Eleven had previously been committed to another institution. They showed a high percentage of psychopathic traits, and we feel that they have unfavorably weighted the whole outpatient group.

Only 3 of the 15 patients are still taking the drug, and we know that one of these had been sober for four months before starting treatment. Two others have remained sober, though they have stopped the drug on medical advice. These 2 patients had remained sober for one and three years respectively before beginning Antabuse, and their reason for taking it at all was largely to encourage the others. The remaining 10 took Antabuse for varying periods: one for six months, two for four months, and two for three months. One gave up the drug because he proposed to get drunk at the Alcoholics Anonymous convention, and the remainder took Antabuse for only a few days or weeks.

There remain 7 private patients referred by their own doctors. Of these, one stopped treatment after less than a month; three have continued steadfast; and three are off the drug for medical reasons. In one man a maniacal reaction developed when his alcoholic crutch was removed, and two others developed hepatitis which we believe to have been due to virus infection and not to the Antabuse/alcohol syndrome. Both these patients have remained sober. We have not seen a case of psychosis due to Antabuse, but we are informed that this sometimes occurs.

Personality Analysis and Selection of Cases

Seven traits characteristic of alcoholic patients[4] were evaluated on the basis of the history, psychiatric examination, and psychometric tests in these patients. The traits are as follows:

1. Anxiety
2. Depressive swings
3. Emotional explosiveness
4. Resentfulness
5. Subjective loneliness
6. Failure to gain social objectives
7. Failure in more intimate interpersonal relationships.

We believe that the distribution pattern

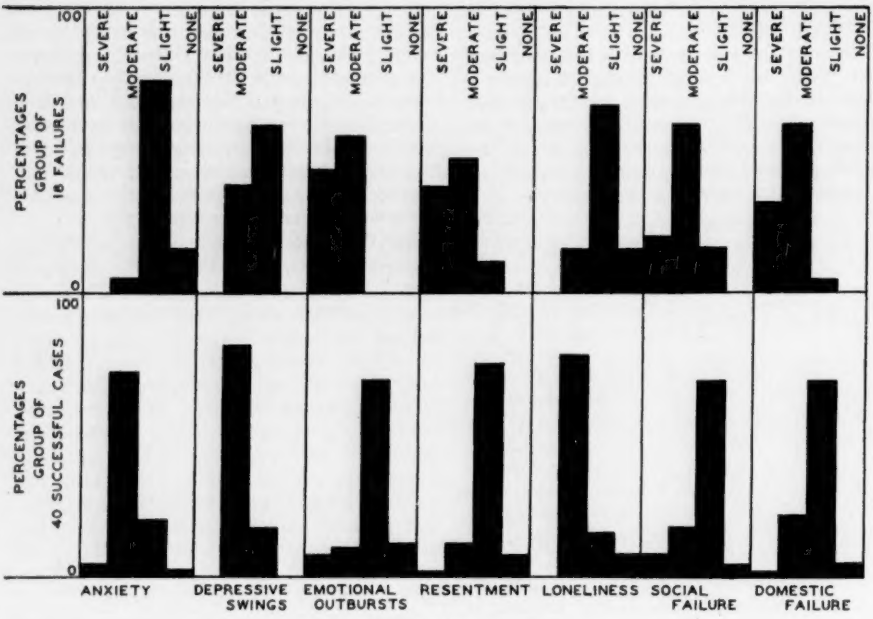

Figure 1

of these characteristics bears some relationship to the prognosis of Antabuse therapy (fig. 1). The presence of moderate to severe anxiety and of moderate feelings of loneliness, and the absence of severe emotional outbursts, resentment, and social and domestic failure are considered to be favorable prognostic signs.

Antabuse is not a cure for alcoholism, but it does support the patient's will to give up the habit. We consider that evidence of this desire is of paramount importance in selecting cases, and this is one of the reasons that a thorough study of the patient in the hospital is desirable. At Graylyn this takes place in a moderately disciplined environment, and the patient's ability to accept this discipline, his preparedness to undertake the expense involved, and his willingness to go through more than one test of his reaction to alcohol are indicative of his will to be well.

We regard explosive emotional reactions, resentment, projective mechanisms, and lack of ability to make reasonably stable interpersonal relationships as evidence of poor prognosis. Such reactions are most often found in aggressive, immature psychopaths, and our experience leads us to believe that these patients are unsuitable for treatment with Antabuse. Patients admitted drunk, or brought to the hospital against their will by anxious relatives, will early reveal their unwillingness to undertake treatment. Others hope for a magical release without realizing that their lasting cooperation is necessary.

The attitude of the family is important, and one looks for stability, intelligence, and patient devotion in the wife or friend as prerequisites to a really satisfactory result. The better the domestic and economic environment, the more secure the patient's future and the greater his chance of recovery.

Physically, the most important contraindications are liver damage and cardiovascular disease, but psychosis or obvious evidence of cerebral deterioration are, we feel, absolute contraindications.

Case Reports

The following case summaries illustrate some of the points made above concerning the selection of cases. The last case is included to show that cases with a most unfavorable prognosis may respond well to Antabuse therapy.

Case 1

A 36 year old white man had been twice married and once divorced. His second wife, a nurse, was a drug addict. He gave a history of having drunk as much as a fifth of whisky a day for fifteen years. He had been admitted to Graylyn on three occasions, and had had two commitments to a state hospital and numerous other admissions to private institutions. A male nurse by vocation, he also has been treated for drug addiction. He had been sentenced for forgery on one occasion.

His mother, a grossly overprotective woman, always gave way to his slightest whim, but he expressed for her a feeling of contempt. His father, an alcoholic, had left the mother when the patient was a child.

The patient was immature, egocentric, and extremely resentful if his unreasonable demands were not acceded to. When sober, he was overbearing and had no sense of guilt about his conduct. He took Antabuse for six weeks only, and was discovered to have substituted Demerol for alcohol during this period.

Case 2

A 33 year old white woman had separated from her husband, an unfaithful alcoholic psychopath, one year ago. He obtained temporary custody of their child. Three years before admission, under the stress of her domestic unhappiness, she had begun drinking as much as two pints of whiskey daily. After separation from her husband she obtained a job where her employer was so impressed with her, in spite of her drunkenness, that he was prepared to pay for her hospitalization and treatment. She recognized on admission that she had a strong motive for giving up alcohol, since the eventual custody of the child would probably depend on her sobriety.

She was a pleasant, cooperative, attractive woman, who accepted the hospital regimen and formed friendships quickly with other patients. Her I. Q. was 108 (Wechsler), and the Rorschach test suggested sensitiveness and feelings of inferiority. There was considerable unconscious hostility, which in the course of psychotherapy became directed toward her husband. She has taken Antabuse faithfully, has cooperated in psychotherapy, is working well, and is coping successfully with her legal problems. She has now been followed for seven months.

Case 3

A 38 year old married white man had been drinking a fifth of whisky per day for ten years. For four months prior to admission he had not left his bed except to obtain supplies of alcohol. He was admitted following an attack of generalized **grand mal**, and was found to have well marked signs of peripheral neuritis. Electroencephalographic studies showed a generalized abnormality but no evidence of a focal lesion.

Psychologic tests showed marked impairment of abstraction and impairment of visuo-motor coordination. Clinically, he showed evidence of organic deterioration. His personality was immature, egocentric, impulsive, and emotionally labile. He had always been indulged by his mother and had never finished his schooling because "he did not like it." His occupational history continued the record of his irresponsibility, and his hobbies revealed his immaturity; he was described as being "always like a child with a new toy."

Antabuse was begun, but was discontinued because of hepatic enlargement. He soon began to drink again, and was readmitted. Antabuse was administered cautiously, and he has remained sober for the past three months. It appears likely that he will continue to do well, because of the devoted support and attention of his wife and doctor.

Summary and Conclusions

1. The routine of therapy employed at Graylyn for patients treated with Antabuse is described.

2. Results obtained in two groups of patients followed for three to eleven months support the view that, in selected cases, Antabuse is a most valuable adjunct to the therapy of chronic alcoholism. Results were less satisfactory in the group treated as outpatients than in the group which was hospitalized.

3. Some factors of importance in prognosis and in the selection of cases are analyzed, and three illustrative case reports are given.

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OBESITY AND HYPERTENSION: THE IMPORTANCE OF A SAFE COMPOUND TO CONTROL APPETITE

Report of a Series of One Hundred Cases

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Although the dangers and handicaps imposed by obesity have been enumerated by many writers, the seriousness of this disease is not fully appreciated. For the physician to disregard pounds of overweight "is ignoring what is perhaps his best chance to lengthen the life and diminish future illnesses of his patient."[1] Actually, a great improvement in the health of the nation appears to be possible by means of the correction and prevention of obesity, for it can be a predisposing or aggravating factor in such conditions as hypertension, varicose veins, nephritis, atherosclerosis, pulmonary emphysema, heart disease, and diabetes[1,2].

Table 1 lists the diseases which I have found to be associated with obesity, and shows the incidence of these diseases in 668

Table 1
Diseases Associated with Obesity

	Incidence	
	Overweight	Normal
Cardiovascular-renal diseases	33%	9%
Myocarditis	14%	5%
Nephritis	12%	4%
Coronary heart disease	4%	2%
Hypertension	15%	8%
Arthritis	12%	11%
Glandular dysfunction (especially male and female climacteric)	3%	3%
Diabetes	2%	2%

obese patients (including the 100 cases in the present series) and a similar number of patients of normal weight. These patients were from all age groups, although the majority (68 per cent) were between 40 and 60 years of age.

The treatment of specific abnormal states in the obese is no different from that in non-obese patients, except that the response to treatment is much more satisfactory when normal weight is attained. Frequently reduction in weight is the only measure needed to correct certain abnormalities. This is particularly true of hypertension[3].

By the treatment of obesity, the physician may ameliorate considerably the effects of many diseases for which no specific treatment is available.

Ray[3b] has stated that "Careful study of the obese who are apparently in good health often reveals subclinical disease directly related to the overweight. Obesity, therefore, if only from the standpoint of preventive medicine, must be regarded as an abnormal and harmful state." Statistical studies indicate that in individuals between the ages of 45 and 50 years, an excess weight of 25 pounds is responsible for a 25 per cent increase in mortality[4]; an excess weight of 50 pounds is responsible for a 56 per cent increase in the death rate; and an excess of 90 pounds increases the death rate by 116 per cent[5]. Thus there is roughly a 1 per cent increase in mortality for every pound of excess weight.

Dublin[6] showed a definite increase in the mortality from all causes in overweight individuals as compared to normal and underweight persons. The most striking differences were noted in the group of cardiovascular-renal diseases. Deaths from this cause among normal, underweight, and overweight individuals occurred in the following proportions: 100:77:162.

Obesity and Hypertension

One of the common complications of obesity is damage to the cardiovascular system. The accumulation of fat around the heart, and occasionally in the myocardium, makes the work of the heart more difficult[7]. Fatty tissue has a rich vascular component, so that the blood must travel a greater distance and frequently must overcome increased peripheral resistance. It is known that increased peripheral resistance raises the blood pressure, and leads to heart disease.

Goldring and Chasis[8] consider a systolic pressure of 150 and a diastolic pressure of 90 as the lower limit of hypertension. By these standards, Rony[9] found hypertension in 19 per cent of his adult obese patients; Gager[10] found systolic hypertension in 28.3 per cent of his obese patients, compared to 16.4 per cent of the patients whose weight was normal. According to insurance statistics, hypertension is two and one-half times more frequent in individuals who are overweight.

In an analysis of 110 obese office patients, ranging from 16 to 61 years of age, Ray[3b] found 35 per cent to have essential hypertension, hypertensive cardiovascular disease, hypertensive retinopathy and nephropathy, coronary insufficiency, and coronary disease. In a similar non-obese group this condition was found in only 10 per cent of the patients. Recently Levy, White and Stroud[11], in a statistical analysis of the medical records of 22,741 officers in the United States Army, showed that the rate for later sustained hypertension was significantly higher in overweight persons than in the control group.

Green and Beckman[7] have raised the question: Is hypertension caused solely by obesity or by an unknown mechanism independent of excess weight, or are both factors responsible? These authors studied 1931 obese patients, and drew the following conclusion: "Hypertension in obese people is not caused by obesity. The same factors which cause hypertension in non-obese people are apparently responsible for abnormally high pressures in the obese. Overweight only aggravates the condition. . . . One of the aggravating factors may be removed by weight reduction, and the prognosis of patients with hypertension is thus improved. Early weight reduction and maintenance of normal weight

are strongly indicated."[11A]

There is no question that obesity increases the incidence of a large number of pathologic processes, and while some of the changes caused by the obesity tend to become irreversible in time, others may be corrected by weight reduction. One of the conditions often amenable to treatment of the obesity is early or mild essential hypertension.

Etiology of Obesity

Various theories have been proposed to account for individual differences in weight. For many decades physicians have been taught that obesity is a glandular or metabolic disturbance. These theories have all been refuted by Newburgh[12] and others, who have been unable to find any alterations in the endocrine or metabolic behavior of obese individuals. Nearly all observers now agree that overweight is simply due to a positive caloric balance, and that obese persons eat more food than they expend in the form of energy.

It must be recognized, however, that obese individuals are victims of circumstance, and their obesity is the result of a perverted appetite. Appetite, as opposed to hunger, is a product of one's environment and is importantly affected by pleasurable and painful experiences. One emotionally disturbed person is distressed by the sight or smell of food (anorexia nervosa), while another finds relief of mental anguish in the pleasurable sensation of a full stomach. This statement does not imply that all or even a majority of obese individuals are emotionally upset. Many are simply the victims of early training and have been conditioned to a higher "satiety level" than is required by the physiologic needs of the body.

Effect of Drastic Food Restriction

By far the most extensive study of cardiovascular dynamics in a population recovering from semistarvation was that done in Leningrad during World War II. A decrease in the blood pressure was one of the characteristic symptoms of semistarvation. Not only was there a reduction in the number of patients hospitalized for hypertension, but there were also significant changes in the clinical picture of hypertension. In a large number of patients with long-standing chronic hypertension, the blood pressure was reduced to a normal or near normal level. Furthermore, symptoms commonly associated with hypertension, such as headaches, dizziness, and dyspnea on exertion decreased in intensity or completely disappeared. In addition to these changes, there was a definite decrease in the severity and frequency of other cardiovascular disorders, such as angina pectoris and myocardial infarction. It is striking to note that in the two years following the famine in Leningrad, hypertension suddenly became a major medical problem.

Brozek and his co-workers[13] confirmed the observations made in the European countries by a wartime research project on cardiovascular degeneration carried out at the University of Minnesota. They also observed striking decreases in blood pressure and pulse rate concomitant with a decline in body weight.

These observations appear to lend support to the concept of treating hypertension by vigorous dietary restriction. Neither study, however, can be regarded as settling the controversy over the relative importance of caloric and sodium restriction in lowering the blood pressure. "If anything, they suggest that caloric restriction may be fully as effective as sodium restriction in producing this result, since in neither the Minnesota experiment nor the Leningrad experience was the sodium intake specifically limited. In fact, the men subjected to experimental limitation of food intake increased their consumption of salt. . . . The salutary effect of weight loss alone in such cases has been repeatedly demonstrated, and a reduction diet rather than a diet of the Kempner type (rice diet) is to be preferred."[13]

The above observations do not warrant the recommendation of drastic dietary restrictions in the treatment of hypertension, but they do offer conclusive evidence of the importance of food restriction in the therapeutic management of hypertension, particularly when the hypertension is associated with obesity.

Management of Obesity

Most types of obesity can be treated simply by a well balanced reduction diet. The restriction of food intake is still the basic principle in all successful attempts at treatment. Dietary restriction over a long period of time, however, is exceedingly difficult in

most cases without the aid of some agent that will depress the appetite. Although many such drugs are being used at present, all of them tend to cause an elevation of blood pressure when administered in the amounts actually required to curb the appetite.

Among the many appetite depressing drugs employed, amphetamine sulfate and desoxyephedrine hydrochloride are perhaps the most widely used. While many investigators have shown experimentally and clinically that these drugs did not materially increase the blood pressure, it must be emphasized that such studies were made with small doses. The dose of racemic amphetamine sulfate used by Harris, Ivy and Searle[14] was 10 to 15 mg. three times a day, while the dose of the dextrorotatory form was half that.

Because desoxyephedrine hydrochloride was used extensively by the German armed forces during World War II, Ivy and Goetzl[15] prepared an extensive review of the German literature. This review indicated that the drug has an action on man and animals similar to that of amphetamine sulfate. It is more potent per miligram than amphetamine sulfate. Golla, Blackburn and Graham[16] compared the effects of amphetamine sulfate and desoxyephedrine hydrochloride on the blood pressure and heart rate in 14 subjects. They found no significant difference in the effects of the two drugs, except that smaller amounts of desoxyephedrine were required. Ten milligrams of desoxyephedrine hydrochloride increased the pulse rate and the blood pressure in 8 and 11 subjects, respectively, and reduced them in 3 and 1 respectively. The maximum rise of blood pressure was 18 mm. of mercury. Frank[17] found that amphetamine sulfate in doses of 10 mg. had no significant effect on blood pressure, whereas doses of 20 mg. increased the pressure for five to seven hours. In a group of patients with fixed hypertension, Pullen[18] found that 6 to 15 mg. of desoxyephedrine hydrochloride caused a sustained rise of 35 to 50 mm. in the blood pressure, the larger rises being due to the larger doses.

Desoxyephedrine hydrochloride and amphetamine sulfate are undoubtedly valuable drugs to diminish appetite in uncomplicated cases of obesity, but one should certainly administer these drugs cautiously in cases of hypertension, particularly hypertension complicated with left ventricular failure or cardiac insufficiency, and severe resistant hypertension.

Warnings against amphetamine for patients with hypertension have been made by the Council on Pharmacy and Chemistry and the Food and Drug Administration. Desoxyephedrine hydrochloride, along with amphetamine sulfate, was placed under the German narcotic, or prescription, law in June, 1941.

The use of thyroid substance for the sole purpose of weight reduction is therapeutically unsound and often harmful[3b]. Thyroid, although long used for the treatment of obesity, raises the metabolic rate, causes a negative nitrogen balance[19], and exerts a direct toxic action on the heart[20]. It is probable that small doses cause undesirable loss of body protein and increase the burden on the cardiovascular system[14-21].

Experience with a Non-Toxic Appetite-Curbing Preparation

Materials

A definite need for a safe means of curbing the appetite and securing weight loss in such severe conditions as hypertension complicated by obesity prompted the search for a harmless, yet reliable, preparation. In a series of 100 cases of hypertension complicated by obesity, Flavettes, a new safe compound to control the appetite*, have been used in conjunction with a diet low in carbohydrates and fats. Flavettes contain in each tablet 1/20 grain of benzocaine aromatized with suitable flavoring extracts in clinically tested proportions, including powdered ginger, licorice, oils of anise, wintergreen, coriander, and cloves. Benzocaine, a local anesthetic, is said to prolong the effect of the various essential oils in curbing the sense of taste. Without benzocaine the action of the oils was too short in duration, and anorexia resulted in only 40 per cent of the cases. With benzocaine, anorexia of longer duration was produced in 80 per cent of the cases[22].

The safety of this compound must be emphasized. Even if the 63 lozenges contained in a bottle were ingested at one time, only a little more than 3 grains of benzocaine would

*Supplied through the courtesy of Amherst Research, Capitol Station, Albany, New York.

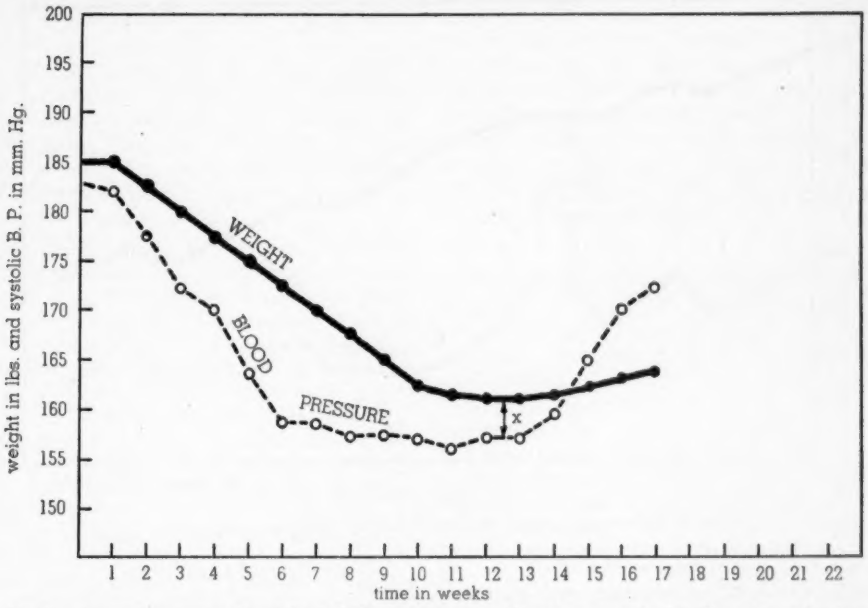

Fig. 1. Average response of weight and blood pressure in 100 cases treated with Flavettes and a low carbohydrate, low fat diet. The sensitivity of the blood pressure to changes in the diet and weight is shown. After several months of the regimen, control is more difficult in a third of the cases, and the curves begin to rise (x).

be taken. The U.S.P. dose is 5 to 8 grains. The flavor extracts are obviously harmless.

Methods

The patient is instructed to dissolve one Flavette on the tongue fifteen to twenty minutes before eating, or whenever he is hungry. The appetite is usually markedly diminished after five to seven days. Administration must be continuous to maintain the initial effect. If the patient objects to the taste, the lozenges may be swallowed. This method was followed in 2 per cent of my cases, and it was found that the results were the same. The exact mechanism of action is not known. It is not the local anesthetic effect alone which is responsible, for results were secured in 40 per cent of one series of cases without benzocaine.

Of the various diets employed for hypertension in connection with Flavettes, the best was a diet low in fats and carbohydrates (less than 15 per cent of each). Less satisfactory was a non-sustaining diet containing from 1000 to 1200 calories, and least effective were the various hypertensive (low sodium) diets. The reducing diets were accepted much more readily when the patient was taking Flavettes.

The patients are told to eat no bread or pastries, no cereal products, and no salad dressing. Lemon juice may be used for salads, and saccharin tablets for sweetening. The following foods may be eaten daily *in any desired quantity* after the appetite is effectively curbed with Flavettes.

Dairy products: Buttermilk, cottage cheese, boiled or poached eggs, milk (whole or skimmed).

Meats: Boiled or broiled, not fried, free from all visible fats; no organs such as kidney, liver, sweetbreads, etc.

Sea food: Fish, crabmeat, lobster, oyster, shrimp; no fried foods.

Fruits: All kinds except bananas, figs, and dates. Remove syrup from all canned fruits and wash with water before serving.

Vegetables: All except potatoes, corn, and lima beans.

Beverages: Water, tea, coffee, milk, vichy, unsweetened fruit juices, pea and tomato soups.

Multiple vitamin capsules were given to

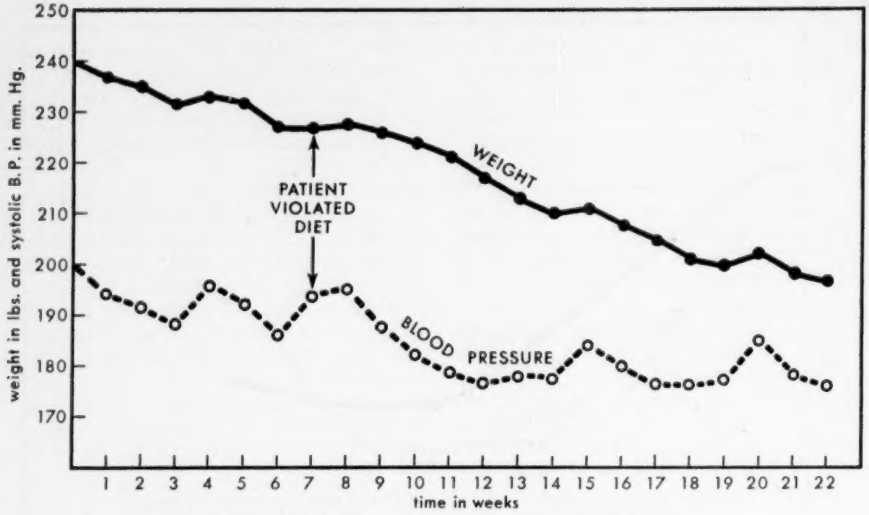

Fig. 2. Relation of weight and systolic blood pressure in case 1

all patients placed on reducing diets.

It is difficult to maintain the desired weight within a range of one pound. My experience shows that the most practical range is 5 pounds. If the desired weight is 150 pounds, the weight could be allowed to vary from 148 to 153. When the individual weighs less than 150, he may eat more freely. As 153 is approached, the stricter diet is enforced.

Results

These cases have been observed for at least three years. The average loss of weight was almost 2 pounds per week for the first eleven weeks, and the fall in blood pressure was proportionate (fig. 1). After several months of the diet, one third of the patients began to gain weight again, and the blood pressure rose sharply. In 8 patients with malignant hypertension the blood pressure, as was to be expected, did not respond to the loss of weight or to any other therapeutic measure which was tried.

In a previous series of 568 cases of obesity complicated by a variety of diseases, excessive appetite was controlled in 80 per cent with the use of Flavettes and a simple reducing diet[22]. Flavettes have been found to be fully as effective as the established appetite-curbing drugs, without producing deleterious effects on blood pressure.

Illustrative Case Reports

Case 1

This 44 year old housewife, the mother of two children, had been known to me for twelve years. Most of her near relatives weighed 200 pounds or more, and her own weight varied between 206 and 247. All of her sisters had hypertension or some other pathologic condition; severe heart disease developed in one. This family impressively illustrates the association of obesity with disease. All of the sisters had a normal basal metabolic rate.

The patient's obesity was evidently the result of an almost uncontrollable weakness for food; she had no will power to resist eating. Her systolic pressure for the past twelve years had varied between 146 and 266; the diastolic, between 84 and 148. The pressure showed a tendency to rise as time progressed. The patient seldom had headaches. On one occasion, however, she complained of extreme vertigo associated with moderate headache, and had to be confined to bed for eleven days. The blood pressure at this time was 266 systolic, 148 diastolic. Except for some weakness on the right side of her body, there were no neurologic findings. The eyegrounds were normal. The electrocardiogram was consistent with hypertensive heart disease.

A faint trace of albumin was present in the urine.

Nitrates, nitrites, sedatives, and a diet low in fat and carbohydrates were prescribed, and Flavettes were given to curb the appetite. After five days, the blood pressure dropped to 200 systolic, 128 diastolic, and after twelve days was found to be as low as 152 systolic, 98 diastolic.

It is interesting to note the fashion in which this patient's hypertension responded to the loss of weight. As soon as she began following a reducing diet, with the aid of Flavettes, her blood pressure dropped, frequently out of all proportion to the actual loss of weight. Decreases of 20 to 30 mm. in systolic pressure, accompanied by a loss of only 2 or 3 pounds, were observed. As she lost more weight (20 to 30 pounds), however, the lower blood pressure range was maintained more steadily.

The primary factors in the successful management of this case appeared to be the caloric restriction made possible by the use of Flavettes. Thyroid, amphetamine, Benzedrine, and similar preparations were considered dangerous in this case.

Case 2

This widow, 68 years of age and the mother of two children, had been under my care for seven years. She had always been obese, her weight ranging from 212 to 305 pounds. When I first took her blood pressure, the systolic pressure went well over the 300 mm. mark, and only the diastolic pressure (158 mm.) could be read. The electrocardiogram indicated an acute and chronic myocarditis consistent with hypertensive heart disease. The patient had infrequent headaches and experienced occasional dizziness.

During the first two years that she was under my care, therapy consisted of the usual hypertensive regimen, including a low sodium diet, nitrites, nitrates, and sedatives. The patient showed so little response—rarely did the systolic pressure come within the visible range of 300 mm.—that I felt this to be a case of essential or malignant hypertension refractory to any medication or other therapy.

The picture changed dramatically after the institution of a diet low in fat and carbohydrates and the administration of Flavettes. During the past five years there has been a marked loss of weight, with a corresponding drop in blood pressure. The systolic pressure has ranged between 300+ and 182, the diastolic from 158 to 114. For the past year the patient has maintained her blood pressure and weight at their lower levels and, to her great satisfaction, on a less restricted diet. She now takes Flavettes only when her appetite requires curbing.

Case 3

A 57 year old merchant, married and the father of one child, had suffered from hypertensive heart disease for years. For the past two years his systolic pressure had varied between 262 and 202, the diastolic between 160 and 108; signs of heart failure began to appear eighteen months ago. The usual hypertensive therapy seemed to be of no avail. On a reducing diet with the use of Flavettes, the patient's weight dropped from 206 to 170 pounds. As is typical of malignant hypertension, however, weight reduction had no effect on the blood pressure. Recently the patient has lost weight as a result of the disease process. The same observation has been made in 7 other patients in this series who had malignant hypertension.

Case 4

A mechanic, 32 years of age and unmarried, came to my office two years ago complaining of weakness, nervousness, and occasional headaches. His blood pressure was 200 systolic, 132 diastolic, and his weight was 240 pounds. Institution of a reducing diet and Flavettes resulted in a gradual loss of weight to 196 pounds, with a concomitant drop in blood pressure to 176 systolic, 80 diastolic. This case was typical of the correlation between obesity and hypertension. Whenever the patient went off his diet, the blood pressure would rise (fig. 2). This case further illustrates the fact that even in a comparatively young individual, obesity may be an important factor in the hypertensive syndrome.

Summary

In a series of 100 cases of hypertension associated with overweight, excellent results were obtained with a diet low in fats and carbohydrates, supported by the use of Flavettes, a new, non-toxic, appetite-curbing preparation. Eight overweight patients with malignant hypertension were not benefited

by this regimen, as was to be expected. Flavettes proved effective in curbing the appetite, and produced no untoward effects.

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Treatment of obesity.—The only way to counteract obesity in the diabetic or any one else, is by a restriction of food intake. In many patients, particularly in some women, the restriction must be severe in order to effect a loss of weight. It may be necessary to limit the diet to 900 calories, or even less, to accomplish any reduction. This is often difficult for the patient and creates at times a psychologic problem which may interfere with continuance or proper adherence to treatment. Those who have overeaten all their lives are naturally self-indulgent, and rigid discipline and breaking of habits of long standing create a serious problem for them.—John, H. J.: Dietary Invalidism, Ann. Int. Med. 32:603 (April) 1950.

PHONOCARDIOGRAMS IN PATENT DUCTUS ARTERIOSUS

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Since 1939, when Gross[1] reported the first successful ligation of a patent ductus arteriosus, interest in all aspects of this congenital anomaly has been quickened. This study concerns recordings of the heart sounds made in 10 patients before and after operation for a patent ductus.

Cardiac Manifestations of Patent Ductus Arteriosus

If the ductus arteriosus remains open after the individual is 4 years old, there is present a continuous "machinery-like" murmur. This is usually harsh, is loudest in the pulmonary area, and is accompanied by accentuation of the pulmonic second sound. A systolic, or sometimes continuous, thrill accompanies the murmur and, like the murmur, is maximal in the pulmonary area. The murmur itself is often so intense as to obscure the second heart sound.

The characteristics of this murmur vary from patient to patient. It has been described as soft, blowing, slightly rough, and loud and roaring. Commonly it is loudest at the beginning of the cardiac cycle, although of 7 cases reported by Jones[2] clear accentuation in systole occurred in only one; in four it was loudest in late systole or early diastole, and in two during diastole. The intensity of the systolic component is reduced in the aortic and apical areas[2,3]. Often the murmur is clearly audible and the thrill easily palpable over the entire precordium, and both may be transmitted to the back and axillae, usually towards the left and to the neck. Sometimes, however, there is little or no transmission of either murmur or thrill and they are easily detectable only in the pulmonic area.

The other cardiac manifestations also vary a great deal. The heart may be normal in size or enlarged to either side or to both sides[2,3,4]. The electrocardiogram is not significantly altered in simple patency of the ductus arteriosus[3], though it may show minor variations of any of the waves[2,3,4a,b,l].

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Axis deviation either to the left or to the right may occur[4d,f,h,i], and depends primarily upon the load placed on the heart and its consequent hypertrophy or degree of failure. The left ventricle pumps from two to four times the volume of blood pumped by the right ventricle[5], but the latter pumps against an increased pulmonary resistance; there is thus an increased load on both chambers. If this is evenly distributed, no axis deviation occurs.

Phonocardiograms

Few phonocardiograms from patients with patent ductus arteriosus have been published. Those which have appeared in the literature may be divided into three general groups as follows:

1. Continuous murmurs with systolic accentuation[3,4f,g,6].

2. Continuous murmurs with accentuation in late systole, early diastole, or both[4e,6,7].

3. Continuous murmurs with diastolic accentuation[2,4a].

From our studies we feel that phonocardiograms are of definite diagnostic value. They also supply permanent records which are useful in comparing the preoperative murmur with those which may commonly persist for variable periods following operative closure of the lumen.

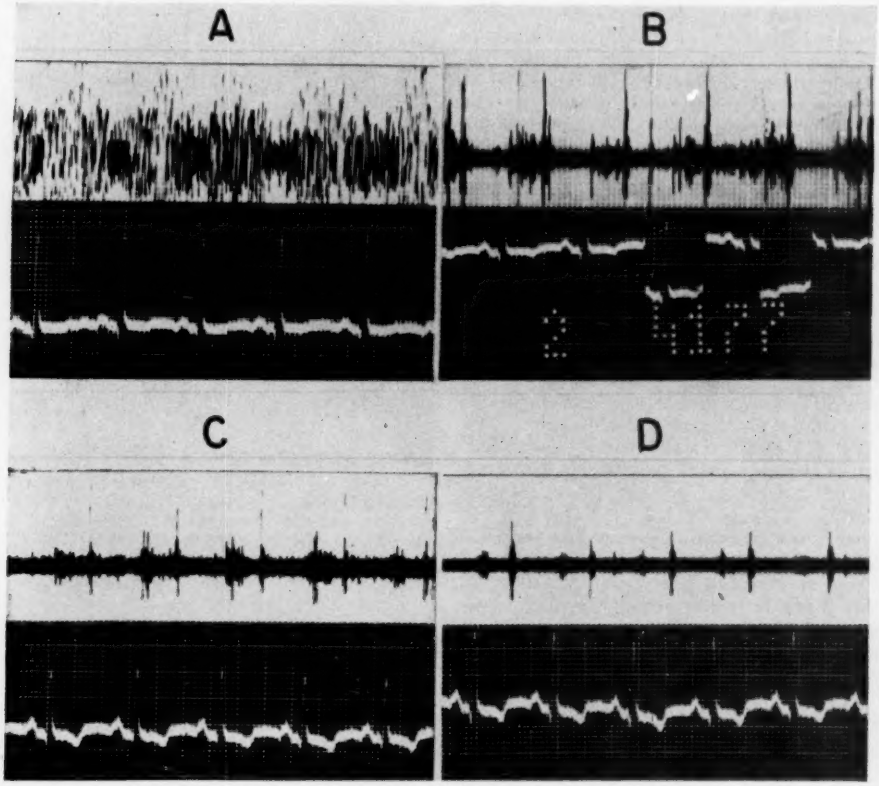

Fig. 1 (Case 1). Phonocardiograms from the left interspace.

A. Preoperative. Continuous murmur which is maximal during systole and early diastole. (Electrocardiographic lead 2).

B. Ten days after operation. (Electrocardiographic lead 2).

C. Fifteen months after operation. (Electrocardiographic lead 3).

D. Twenty-two months after operation. (Electrocardiographic lead 3). Note the accentuation of the pulmonic second sound in the postoperative records.

Findings in Patients Treated at Duke Hospital

The tracings presented were made from patients admitted to Duke Hospital, all of whom had an operation to close the shunt. Most of the records were taken by means of the sound and pulse capsules devised by Wiggers[8]. In two patients the Cambridge instrument was used.

The presenting complaint in most cases was dyspnea and excessive fatigue with moderate exertion. No patient exhibited cyanosis or arrhythmia except for a few occasional premature systoles. Following operation there were few significant alterations in the blood pressure levels. Systolic pressures range from below normal to above normal, and pulse pressures are usually increased because of the lower diastolic pressure. In these cases the preoperative systolic pressures tended to be high, and in all except two the diastolic pressures were lower than the commonly accepted values for corresponding ages. At operation it was observed that the diastolic pressures rose immediately after the ductus was closed. Heart rates were not significantly altered. Teleroentgenograms showed either moderate enlargement or no enlargement of the heart, and the electrocardiograms showed no significant alteration.

Phonocardiograms of 5 patients are shown in figures 1-5. The varying characteristics of the murmurs in the phases of the cardiac cycle are clearly illustrated, and form the basis of the discussion which follows.

Table 1 lists the outstanding characteristics of the murmurs and thrills observed. The disappearance of the murmur postoperatively is of considerable interest. In general, the pulmonic murmur has persisted longest. A grade 1 pulmonic murmur lasted to the seventeenth postoperative month in cases 3 and 5. In the former the ductus was ruptured during the operation, and there was some doubt as to whether it had been completely occluded. The murmur became, however, progressively less intense and disappeared completely from the aortic area.

Comment

Phase of maximum intensity of the murmur

Murmurs are generally considered to be the result of turbulence of the blood stream in the heart and blood vessels. It is assumed that maximal turbulence coincides with maximal blood pressure and velocity — which, in the healthy cardiovascular system, occurs during the phase of maximum ejection of the heart. Thus one would expect the continuous murmur caused by a patent ductus to be loudest during that period, and it is usually so described.

Both clinical experience and phonocardiographic records, however, indicate that the two maxima often do not coincide[2,4a,6,7]. From our own phonocardiograms and auscultation of the patients in this series, it appears that maximal intensity of the murmur does not necessarily occur at the ex-

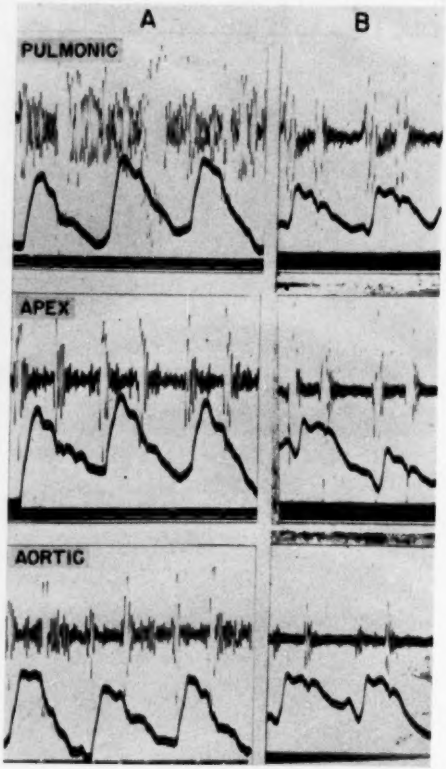

Fig. 2 (Case 2). Phonocardiograms and carotid pulse (time, 0.2 sec.)

A. Preoperative. A grade 3 pulmonic murmur is maximal after the second heart sound. The second pulmonic sound is accentuated.

B. Postoperative pulmonic murmur, grade 1, is maximal in systole. The second pulmonic sound is accentuated. Note the absence of the murmur postoperatively in the aortic and apical areas.

pected time of maximal turbulence. Furthermore, the phonocardiograms show that the murmur may be loudest in any part of the cardiac cycle, though it is usually maximal in late systole or in both late systole and early diastole. Thus any attempt to explain the intensity of the murmur by existing pressure or velocity differences will fail in many instances.

Cournand and others[9] found that pressures in the right ventricle of 8 normal subjects ranged from 18 to 28 mm. of mercury, the average being 22 mm. This finding would indicate a pressure difference of approximately 5 to 1 between the aorta and the pulmonary artery, although no measurements of systemic pressure were published. Furthermore, considerable differences from the normal flow were reported by Eppinger and Burwell[5], who used data obtained from Gross's patients before and after operation. They estimated that from 45 to 75 per cent of the blood pumped out by the left ventricle into the aorta passed back into the pulmonary circuit through the ductus. The left ventricle therefore pumped from two to four times as much blood as was pumped out during the same time by the right.

This observation has been confirmed in some patients by Steinberg's angiocardiographic study of 27 cases. Steinberg and his coworkers[41] wrote:

> "It was expected that the shunt of blood from the aorta to the pulmonary artery would result in continuous visualization of the pulmonary vascular tree since the pressure in the aorta is much higher than in the pulmonary artery . . . ." "In a few of our cases there did indeed appear to be a slight but distinct persistence of opacification . . . . This finding must therefore be interpreted with considerable caution."

The assumption that the shunt is from the aorta to the pulmonary artery was questioned by Hunter[10], who observed the blood flowing in two patients in whom the ductus was very thin. His impression was that in both cases the flow was from the pulmonary artery into the aorta. He admitted that, "This is against all the views previously expressed, but those views have been largely theoretical." He presented some indirect evidence in support of his view. In a discussion of this paper, Tubbs (p. 110) expressed the opinion that Hunter's "novel suggestion" should not be maintained, and cited direct and indirect evidence supporting the classical view. Eppinger, Burwell and Gross[11] have also produced in experimental animals an arterial communication between the aorta

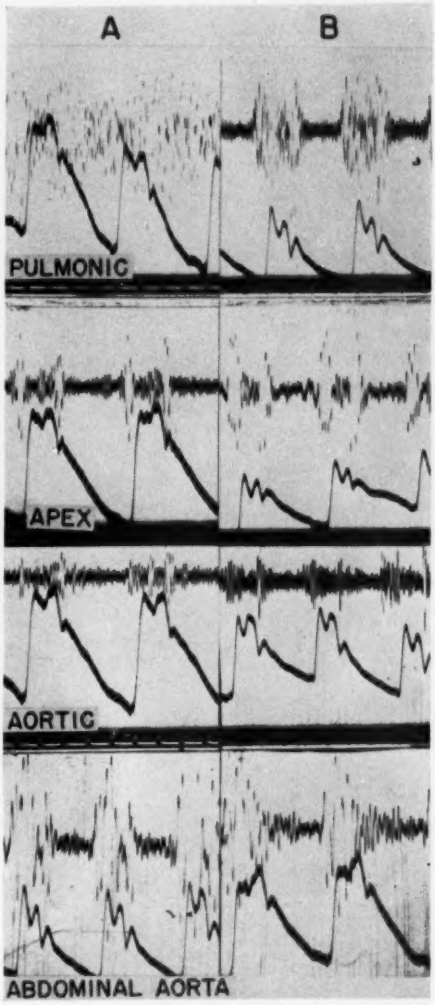

Fig 3 (Case 4).

A. Preoperative records: phonocardiogram and carotid pulse (time 0.2 sec.). The grade 4 pulmonic murmur is maximal in late systole and early diastole, and in mid to late systole in the apical and aortic areas. From the abdominal aorta a maximal rough systolic rumble louder than in the pulmonic area was heard, followed by a faint diastolic murmur.

B. Records taken on the fourteenth postoperative day. From the pulmonic area a systolic murmur persisted which was less harsh and more blowing in character. The diastolic component was faint. From the abdominal aorta the intensity of the systolic murmur was unchanged; the diastolic portion was slightly louder.

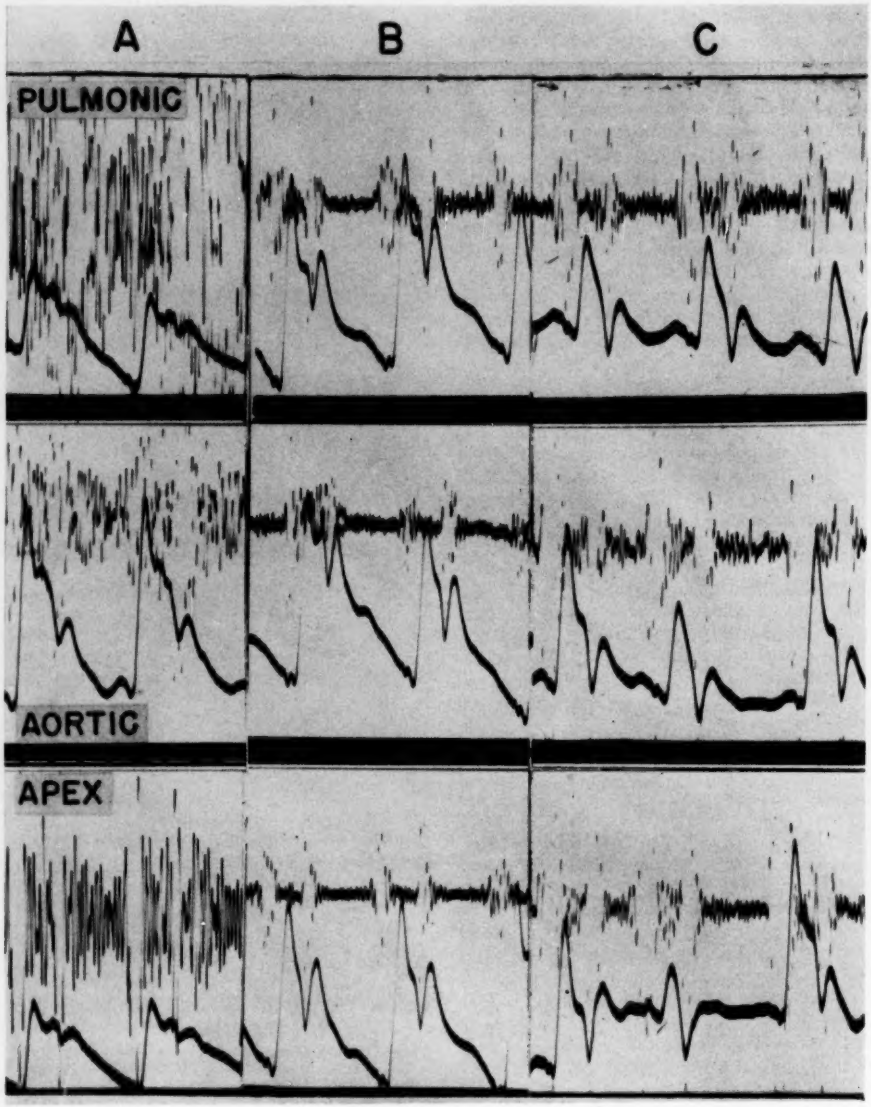

Fig. 4 (Case 5).

A. Preoperative records. Each record shows heart sounds and carotid pulse (time, 0.2 sec.). The murmur is continuous and "machinery like," maximal in the pulmonic area during late systole and early diastole. The sound capsule was maximally damped.

B. Postoperative records on the fourteenth day. Only a faint systolic murmur (maximal in the pulmonic area) is evident.

C. Nine months after operation. There was little change in the intensity of the murmur as compared with B. The patient at this time had numerous premature auricular systoles varying from 1:5 to 1:1.

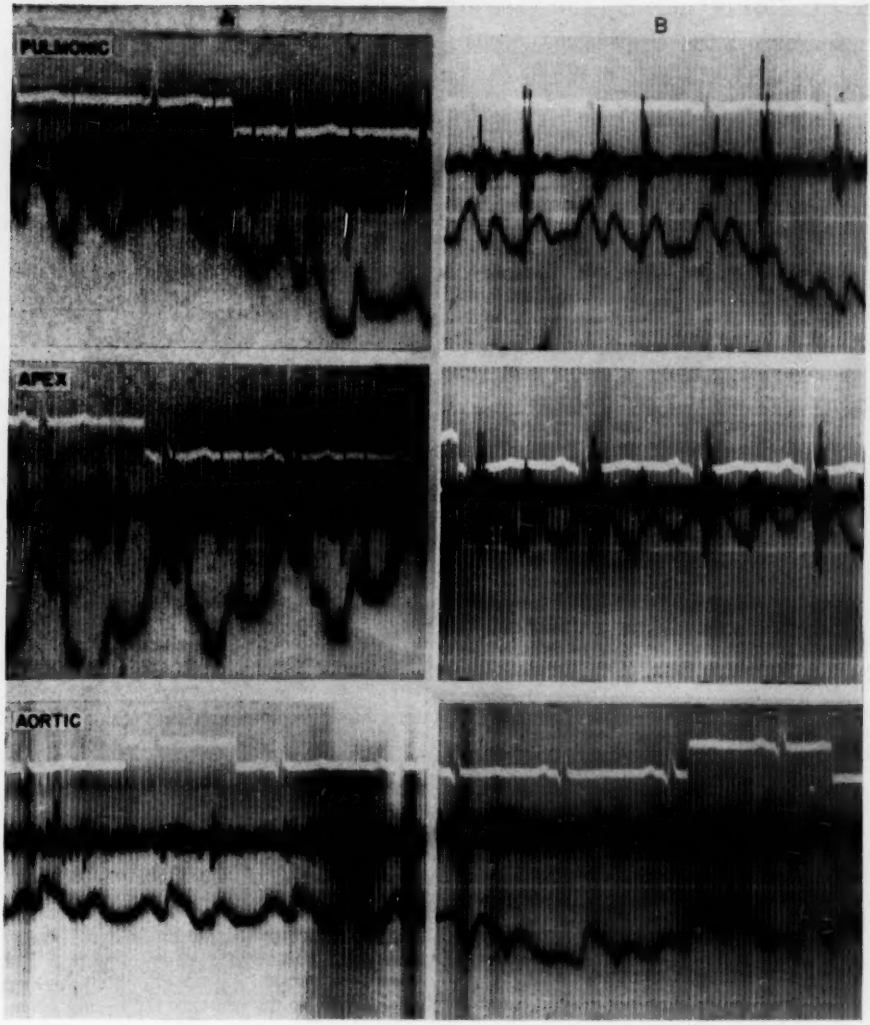

Fig. 5 (Case 9).

A. Preoperative records. From top to bottom: pulmonic area, electrocardiographic lead 1; apex, electrocardiographic lead 2; aortic area, lead 3. There was a continuous murmur, maximal in diastole. The apex record shows a loud third heart sound. The pulse tracing is from the right jugular vein.

B. Postoperative records on the twelfth day. Electrocardiographic leads from each area are the same as in A. A grade 1 pulmonic murmur is maximal in systole. The third heart sound has disappeared at the apex.

Table 1

		PREOPERATIVE								POSTOPERATIVE (AT DISCHARGE)						
										Grade of Murmur				Postoperative Persistence of the Murmur in Months		
Case		2nd left I.S	3rd left I.S	Aortic Area	Apex	Left Axilla	Back	Phase of Cycle when Pulmonic Murmur Was Loudest	P_2 Obscured	Pulmonic Area	Aortic Area	Apex	Phase of Cycle when Pulmonic Murmur Was Loudest	Pulmonic Area	Aortic Area	Apex
1	M	4	4	2	1	0	0							+15	+9	−9
	T	2	2	0	0	0	0	S;ED	Yes	2	1	1	S	−22	−15	−15
2	M	3	3	2	1	1	0		Some					+3	+½	−½
	T	2	1	0	0	1	0	ED+D	Cycles	2	0	0	S	−6	−3	−3
3	M	3	3	2	2	0	0				very					
	T	2	2	0	0	0	0	S	No	1	slight	0	S	+17	−17	−17
4	M	4	3	1	1	2	1									
	T	3	3	0	0	1	0	ED+D	Yes	3	1	1	S	———	———	———
5	M	6	5	3	3	2	1	S						+17	−8	+8
	T	4	4	0	0	1	0	ED	Yes	1	1	0	S			−13
6	M	3	3	2	2	2	2									
	T	2	2	0	0	1	1	ED	Yes	1	1	1	S	Failed to return		
7	M	4	3	3	1	0	0									
	T	2	2	0	0	0	0	LS;ED	Yes	3	2	1	S	Failed to return		
8	M	2	2	0	0	0	0									
	T	0	0	0	0	0	0	ED	No	1	0	0	D	Failed to return		
9	M	3	2	2	2	1	1									
	T	2	1	0	0	0	0	D	No	1	1	1	S	Failed to return		
10	M	4	3	2	2	1	1									
	T	2	1	0	0	0	0	S+ED	Yes	1	1	0	S	Failed to return		

Legend:
Interspace = I.S.
Cardiac Murmur = M (Grade 1-6)
Cardiac Thrill = T (Grade 1-4)
Systole = S
Late Systole = LS
Diastole = D
Early Diastole = ED

\+ = Persistent
− = Absent

and pulmonary artery. Their evidence supports only the concept of a continuous blood flow from the aorta through the artificial "ductus" in both the systolic and diastolic phases of the cardiac cycle.

Since most published observations indicate that the maximal murmur should be systolic, other possible explanations for variations in the intensity of the murmur during the heart cycle must be examined.

Turbulence may develop slowly and persist for a short time after maximal pressure and velocity are reached. This fact may account for a late systolic and early diastolic accentuation of the murmur.

It is possible that the movement of the heart during systole may produce some torsion upon the ductus, thereby reducing the rate and volume of flow through the ductus during the systolic phase. This would reduce the intensity of the systolic murmur. Furthermore, in certain patients, transmission of the murmur in systole and diastole may differ. This phenomenon also could be due to a change in the position of the heart during systole, which might alter transmission of sounds to the chest wall.

Theoretically, a flow from the aorta to the pulmonary artery would increase the pulmonary blood volume and the pulmonary arterial pressure, with a resultant increase in the force of the contraction of the right ventricle. This in turn would cause some elevation of the pulmonary systolic arterial pressure. Should this rise be fairly large, it would impede systolic flow from the aorta into the pulmonary artery, and so could reduce the turbulence and the intensity of the systolic murmur. Since the normal resistance of the pulmonary bed is low, the flow in diastole would be proportionately less impeded, and might account for a real or apparent diastolic accentuation. In our opinion, however, neither possibility offers a satisfactory explanation for the mid-diastolic accentuation of the murmur.

Course of postoperative murmurs

At the time of discharge all patients had systolic murmurs of slight or moderate intensity. Only one patient had a continuous murmur, and this had completely disappeared in eighteen months. We believe that this murmur is due to the fact that ligation

of the ductus causes a "dimpling" of the aortic and pulmonary arterial walls, which interrupts their smooth contour and sets up turbulence at those points. As the dimpling is gradually and smoothly filled in during the healing process, the murmur disappears. Indirect evidence supporting this thesis arises from the fact that in every case which we have been able to follow, except one, the murmur has completely disappeared, and that in this one case its intensity has progressively decreased.

Summary

The characteristics of the phonocardiograms in 10 cases of patent ductus arteriosus are tabulated, and some of the phonocardiograms are illustrated. Certain aspects of the variation in the murmurs throughout the cardiac cycle, and possible reasons for these variations, are further discussed.

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OPERATIVE RESULTS IN PROSTATIC SURGERY

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In the two and one half years from January 1, 1947 to July 1, 1949, 160 prostatic operations have been performed by my associate, Dr. Thomas R. Huffines, or myself. In this series of 160 cases there was only one postoperative death—a mortality rate of 0.6 per cent. In similar studies reported in the literature the average mortality for all types of prostatic operations has ranged between 3 and 4 per cent[1].

We have done approximately twice as many transurethral prostatic resections as suprapubic prostatectomies. One hundred and nine resections, 50 suprapubic prostatectomies, and one perineal prostatectomy were performed. We routinely perform the suprapubic prostatectomies in two stages, despite the fact that many urologists are doing them in one stage. Although the hospital stay is lengthened, we feel that both mortality and morbidity are less with the two-stage method.

The rest of the figures do not include data on 17 cases that are included in the statistics just given. These 17 operations (15 resections and 2 suprapubic enucleations) were performed by Dr. Huffines at the Swannanoa Division of the Oteen Veteran's Hospital. The same techniques were followed in these cases, and it is safe to assume that inclusion of the data from them would not have changed the over-all picture materially. The other operations were all done in various Asheville hospitals.

Only 14 of the 143 patients had malignant lesions of the prostate. All of them were too far advanced for hope of a permanent cure.

The average age of our patients was 69; the oldest patient was 90 and the youngest 51.

Choice of Operation

In our transurethral resections an average of 16 Gm. of prostatic tissue was removed. The largest amount was 61 Gm., and the smallest just one or two bites. The average weight of tissue removed by prostatectomy was 59 Gm. Other factors being equal, we perform resections on all patients whose

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glands are small enough so that a complete resection can be carried out in a period of one hour or less. In all other cases we carry out the enucleation. In only one of these cases has a second resection been necessary. That patient's prostate was benign histologically at first, but the tissue removed the second time was malignant.

It will be noted that we have not performed any retropubic prostatectomies. In this operation, which was introduced in England two years ago, the prostate is approached anteriorly and inferior to the bladder, in the area underneath the symphysis pubis. Since its introduction, this operation has attracted more attention than any other in the field of urology. We have two reasons for not having used it. First, Millin, the originator and acknowledged expert, had a mortality of 4.75 per cent[2] in his first 600 cases. Since our mortality is much lower, we naturally are hesitant to try the new procedure. Second, neither one of us has witnessed enough of these operations to feel that we have learned the technique. When the experts can show a better record, and when we feel competent in the operation, we shall use it in appropriate cases.

Preoperative Preparation

Possibly the biggest factor in the successful performance of prostatic surgery is the preoperative preparation. We are dealing with elderly men who have impaired circulation, often impairment of kidney function, and occasionally senile mental changes. In no other type of surgery is it more important to consider the patient as a whole. If there is evidence of renal damage, we will not operate until the kidney function is restored to normal, or nearly so. Of equal or greater importance is the patient's cardiovascular status. In our series of 143 patients, 41 had hypertension, congestive failure, definite coronary disease, or a combination of these conditions. In a sense all of the patients could be considered at least potential candidates for cardiac disease. Certainly their circulation and tolerance were poorer than those of younger patients. For these reasons, practically every patient in this series was examined by a cardiologist, and had at least a plain film of the chest and an electrocardiogram made.

Our preoperative routine is as follows: When the patient is admitted, an indwelling catheter is inserted if he is carrying residual urine, has an undue amount of infection, or is uremic. In addition to the routine laboratory procedures, a Wassermann test and determination of the blood nonprotein nitrogen, blood sugar, and sedimentation rate are made. Plain roentgenograms of the chest and abdomen are obtained. General supportive therapy consists in the administration of ample fluids and accessory vitamins; the patient is allowed to be ambulatory if his condition permits. He is seen in consultation by a cardiologist, and an electrocardiogram is obtained. If any of these procedures reveals a condition which can and should be ameliorated before operation, then the indicated therapy is carried out, regardless of the time required.

Operative Procedure

I will not give a detailed description of our operative technique, but will only say that we try conscientiously to do the best job possible, and in the resections endeavor to remove all tissue down to the capsule, just as is done in the enucleations. At the conclusion of either a resection or the first stage of the prostatectomy, we routinely ligate the vasa in order to prevent epididymitis. When this routine is neglected, the incidence of this complication is too high, in spite of routine postoperative chemotherapy. Spinal anesthesia with Pontocaine is used for most of the resections, and every effort is made to keep the blood pressure from falling. For the prostatectomies cyclopropane or a combination of oxygen and ether is used. It may well be that the ability of our anesthetists is more important than the choice of the agent. To them belongs a great deal of the credit for our good results.

Postoperative Care

Immediately after the patient returns to the ward, he receives a transfusion of whole blood. I do not believe that this procedure is carried out routinely in many clinics. Most of the patients do not actually need the blood, but we believe that the transfusion is worth while, even in that group. Their strength is maintained, and they recover more rapidly. Quite frequently, if there is any question about a patient's cardiac status, we also employ an oxygen tent prophylactically for the first twenty-four or forty-eight hours. This precaution, too, pays dividends. Supportive therapy is maintained throughout the patient's hospital stay.

About two years ago we realized that postoperative thromboembolic complications were occurring too often in our patients. An analysis of all the major urologic operations performed in the year 1947 showed that 7 per cent of the patients had some form of thrombosis. From the lessons we learned in that study, we have succeeded in reducing the incidence of thromboembolic disease following prostatic operations to 4 per cent. This improvement can probably be attributed to the adoption of simple, but fundamental, routines. We made certain that the patients had both active and passive exercise in bed, and were made ambulatory as soon as possible. In 1947, before we started concentrating on this problem, the average period of complete bed rest following a transurethral resection was 3.4 days. Since January 1, 1948, we have succeeded in getting these patients up within 2.6 days, on the average. Including the time interval in bed following both stages of the suprapubic prostatectomies, the average period of bed rest for each patient has been reduced from 20.2 days in 1947 to 16 days since January 1, 1948.

Our criteria for the discharge of the patient are as rigid as the preoperative preparation. We keep patients for two weeks following a resection. While they are physically able to go home long before this, we have learned from bitter experience that the risk of bleeding at home is too great if they are allowed to leave the hospital earlier. We do not feel that an early discharge is worth the risk, especially since many of our patients come from remote towns or rural areas. Following a suprapubic operation, we insist that the wound be completely healed and that there be no leakage of urine before the patient is allowed to leave.

Explanation of Fatality

A word must be said concerning our one death and the apparent cause. The patient was fundamentally average in all respects. A transurethral resection was carried out, and 8 Gm. of tissue removed. Toward the end of the resection, when the prostatic capsule was reached, a venous sinus was opened. Considerable time was spent in fulgurating the area, but moderate bleeding persisted. It was controlled to a safe extent, however, by traction on a balloon catheter. The patient received the routine postoperative transfusion, and seemed to be in good condition for about six hours. There was no undue bleeding. At the end of that time, however, he went into severe shock. In spite of two more transfusions and several units of plasma, he expired about twenty-four hours after the operation. No autopsy was obtained.

In the past two years, urologists have come to recognize a syndrome of varying severity which follows prostatic surgery and is characterized by shock, oliguria, nausea and vomiting, jaundice, and uremia. In such cases, as in our case, there had been bleeding from a venous sinus in the prostatic capsule during the resection. It seems logical to assume that this syndrome is caused by an intravenous infusion of sterile distilled water which is routinely used as an irrigating medium. This medium can easily reach a pressure in the prostatic fossa which is greater than the patient's venous pressure. The water presumably causes hemolysis, hemoglobinemia and hemoglobinuria, to explain the symptoms described above.

There still remains the possibility that our patient's first transfusion was incompatible. This possibility was explored at the time, however, and no break in the usual matching procedure could be detected.

Needless to say, we are making every effort to avoid this hemoglobinemia syndrome. The obvious prophylactic measures are: (1) to avoid cutting the prostatic capsule; (2) to allow the irrigating medium to drain out before the bladder has become distended; and (3) to keep the flask containing the water at as low a level as possible. Different irrigating media have been devised which are isotonic and which would be harmless if accidentally introduced into the blood stream. The most popular of these is a 4 per cent solution of glucose. When this is used, however, serial blood sugar determinations and appropriate coverage with insulin are required. Our present laboratory situation precludes the use of this technique. Another solution, made up of amino acids and glycine, avoids the complications of glucose, but is very expensive. For the present, we are relying solely on our precautions in the operative technique.

Late Results

We have been able to follow most of our patients very well. We are proud to say that in this series there has not been a single case of incontinence, the *"bete noire"* of all

prostatic surgeons. Some of the patients have had temporary incomplete incontinence, but all of them have regained complete control in a short time.

Perusal of our late results does reveal the too frequent occurrence of an annoying complication. Urethral strictures have developed in 11, or 7 per cent, of the patients. Fortunately they are not serious and can be dilated easily. Again, the best treatment is prophylaxis. We are paying more attention to having the sheath of the resectoscope well lubricated. We do a urethral meatotomy in all cases where the meatus is at all tight, and we use the size 24 F. resectoscope whenever the urethra as a whole is too tight on the size 28 F.

The only other noteworthy postoperative complication in this series was bleeding which occurred in 3 patients after their return home, and was sufficient to require hospitalization to stop it.

Conclusion

It is obvious that if any one word could be applied to our handling of these patients, it is "conservatism." We are often tempted to take short cuts, or to omit parts of our established routine. Every time we start to slip on one detail or another, however, our error is soon brought home to us.

I cannot finish without reiterating the importance of instituting proper treatment early in these cases. It is manifest, in both the benign and the malignant cases, that early treatment will save untold suffering and prevent many deaths.

Finally, in order to give credit where it is due, I must say that most of these routines have been worked out from experience by my associate, Dr. Huffines. The fundamentals are observed universally, but he deserves credit for sticking to several of the conservative practices which others recommend discarding. We have no intention of remaining static, however, and when the value of new departures has been irrevocably proven, we shall adopt them.

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THE MODERN TREATMENT OF TYPHOID FEVER

With Report of a Case

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Typhoid fever is a most remarkable disease which has been known almost since the beginning of medical history. The story of the gradual recognition of this disease and the associated discoveries[1] is a fascinating tribute to the perseverance, knowledge, and common sense of the doctors who brought these things to pass. Gerhard, a brilliant young student of the great Louis, was the first to give us an accurate differentiation of typhoid and typhus. The organism that caused typhoid was discovered by Eberth in 1800. Typhoid vaccine was first used in 1896 by Pfieffer and Kölle, and two years later by Wright. This achievement, together with sanitation, has made typhoid fever a rare disease in this modern age. It would seem possible that modern sanitation and the vaccine could entirely do away with typhoid fever as a disease entity. It is probable that in this country the carrier is now our main source of danger.

Chloromycetin

While this tremendous progress was being made toward preventing typhoid, nothing was being accomplished in the way of specific treatment. Until very recently, the treatment consisted entirely of general measures. With the introduction of Chloromycetin, however, it looks as though therapy has at last caught up with prophylaxis in typhoid fever. This antibiotic, which has marked antibacterial activity against several gram-negative bacteria[2], but is inactive against yeast and other filamentous fungi[3], was first used to treat typhoid fever in Bolivia in 1947[4].

In July, 1948, Woodward and others[5] reported on the use of the drug in 10 cases of typhoid seen in Malaya. Eight cases were used as controls. The average duration of fever in the 10 cases treated with Chloromycetin was 12.5 days, or 3.5 days from the beginning of treatment. (The patients had had fever for an average of nine days when the drug was started.) In 8 of the 10 cases,

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blood cultures were taken daily for five days after initiating treatment. They remained sterile. In 2 of the cases blood cultures were taken at two, four, and eight hours after the first dose of Chloromycetin. These too remained sterile*. Relapses, which occurred in 2 of the 10 cases after fourteen and sixteen afebrile days respectively, responded promptly to a second course of Chloromycetin.

One of the 8 control cases died of the disease. The average duration of fever in the remaining 7 cases was thirty-five days.

Smadel and others[6] have reported the treatment of 44 cases of typhoid fever by means of Chloromycetin. Each patient received an initial dose of 3 to 4 Gm., then 1 to 3 Gm. daily in divided doses. In one group of 13 patients treated for 6.9 days there were 7 relapses. No relapses occurred in the remaining patients, who were treated for 11.2 days or more. It was concluded that Chloromycetin should be given for more than eight days in adequate doses.

Woodward[7] and others have reported that the usual complications of typhoid may occur during or after treatment with Chloromycetin, even after the fever has subsided.

Dosage

According to Dr. R. J. Buckman, of Parke, Davis, & Company[8], "Initial dosage in the acute phase should be calculated on the basis of 50 to 60 mg. per kilogram of body weight, followed by 0.25 gram every two to four hours until there is normal temperature." He further recommends that the Chloromycetin be given for not less than eight to ten days, in doses of 0.25 Gm. every four to six hours during the afebrile period, and in higher doses if the blood cultures remain positive. For a relapse, he recommended the administration of 3 Gm. daily for three to five days, or more as dictated by the condition of the patient.

It has been found that Chloromycetin disappears very rapidly from the blood, and for this reason has to be given often[9]. Woodward[10], in explaining the action of Chloromycetin, states that the drug apparently suppresses the growth of the typhoid organisms and that final recovery seems to depend on the development of immunity in the host. According to Parke, Davis, & Company, manufacturers of the drug[4], Chloromycetin in clinical concentrations is bacteriostatic but not highly bactericidal to *Salmonella typhosa*. The manufacturers also state that Chloromycetin is effective not only in typhoid fever, but also in the paratyphoids.

Toxic effects

In therapeutic dosage, the drug is said to be free from toxic or undesirable effects. However, 2 cases of reversible leukopenia and granulocytopenia, apparently due to Chloromycetin, have been reported[11], and in 3 reported cases[12] a severe granulopenia and a granulocytic hypoplasia with both erythroid and granulocytic maturation arrest in the bone marrow followed Chloromycetin therapy.

One drawback which Chloromycetin seems to have in common with some of the other antibiotics, and particularly Aureomycin, is that it disturbs the normal intestinal flora at times, and permits the Monilia, over which it has no influence, to grow wild. The parenteral or oral use of the vitamin B complex should be helpful in this condition. If diarrhea is present, the judicious use of belladonna may be advisable.

The stomatitis, anal irritation, and vaginitis which are sometimes associated with the use of antibiotics resemble an acute vitamin B deficiency, and in fact this is probably the true explanation. The bacteria which ordinarily aid in the synthesis of the B complex are destroyed by the antibiotic. In addition a Monilia infection is often superimposed, because the absence of normal intestinal flora and the lowered resistance of the mucosa permit this fungus to grow at will.

I saw and helped to treat an elderly woman with typhoid fever, in whom stomatitis developed after a five day course of Chloromycetin. Her mouth and tongue were red, and Monilia was obtained on culture. After a few days of intensive therapy with the vitamin B complex, the stomatitis cleared up.

Treatment of carriers

There seems to be some difference of opinion as to the effect of Chloromycetin in clearing up the carrier state. Erickson[13] has reported that a carrier with a positive stool culture was cleared up by the use of Chloromycetin. In a case treated by Collins[14] the stools became negative during treatment, but reverted to positive after treatment.

According to Dr. Buckman[8], the treatment of carriers should consist in giving 100

* Gabinus (Lancet 2:866 (Nov. 5) 1949), remarking on the rapidity with which the cultures become negative following administration of the drug, said that the Chloromycetin in the blood sample itself was responsible.

to 150 mg. of Chloromycetin per kilogram of body weight daily, in four to six equally divided doses. He suggested giving the drug in several courses of ten to fourteen days each, separated by intervals of a week or ten days.

Report of Case

The purpose of reporting the following case is not only to illustrate the effectiveness of Chloromycetin in the treatment of typhoid fever, but also to call attention to the fact that this disease, although rare, must still be considered in the diagnosis of any unexplained fever.

A 20 year old unmarried white woman was admitted to Watts Hospital on December 30, 1949, with the chief complaint of chills, fever, and malaise for the past two days. She stated that she had had headache and generalized aching three weeks before admission, and thought she was taking "flu." These symptoms disappeared, but recurred one week before admission. She was able to continue working a few days longer, but was then forced to go to bed and call her doctor. She was given some penicillin, but continued to get worse. She was told that she had virus pneumonia and was given more penicillin, together with Aureomycin and a sulfonamide drug. She began to have chills and diarrhea, and was sent to the hospital. She had no cough or pain.

The patient had had mumps, whooping cough, chickenpox, and "both kinds of measles" in childhood. There was no history of rheumatic, scarlet or typhoid fever, or of diphtheria. She had had no operations.

The patient worked at a beauty parlor and lived in town. She ate regularly at a cafe. The family history was negative. The mother, father, and three brothers were living.

Physical examination on admission showed a well developed, rather obese young white woman in no acute distress. The temperature was 101.6 F., the pulse 108, blood pressure 120 systolic, 80 diastolic. The tonsils were enlarged and the pharynx was reddened. There was some impairment of resonance over the lower right lung; breath sounds were louder at the left base than at the right; some crackling and moist rales were heard over the left base and in the left axilla. The heart was apparently normal, as were the eyes and ears, neck, abdomen, breasts, extremities, and reflexes. Rectal examination was negative.

The tentative diagnosis was probable virus pneumonitis, upper respiratory infection, diseased tonsils, and obesity.

Accessory clinical findings: On admission the urine showed a 3 plus reaction for albumin, many granular and leukocytic casts, 10-12 white blood cells per high power field, with clumps, and an occasional red blood cell. The hemoglobin was 82 per cent, the red cell count 4,400,000, white cell count 4650, with a normal differential. Kahn and Mazzini tests were negative. Agglutination tests were positive in the following dilutions: **Eberthella typhosa** H—1:400, O—1:200; **Salmonella paratyphi** —1:80; **S. schottmülleri**—1:80; heterophile—1:28; undulant fever—1:80; Weil-Felix—1:40. An agglutination test for tularemia was negative, and there were no cold agglutinins. The sedimentation rate (corrected) was 25 mm. in an hour. Blood urea, urea nitrogen, and sugar were normal. No malaria parasites were found.

A portable film of the chest made on admission showed "some infiltration about both hila and in the lower portions of the right lung. The appearance is consistent with an early atypical pneumonia." A portable film of the chest made the next day showed the lungs to be essentially clear.

A urologic consultation was obtained on January 1 (two days after admission). The consultant's impression was: "Some inflammatory process in the urinary tract which may be either a pyelonephritis or a nephritis, probably a secondary response."

Course in the hospital: The patient continued to have chills, and her temperature varied from 98 to 105 F., averaging about 102 F. for eight days. One pinkish spot was seen on the abdomen. There was no glandular enlargement. The abdomen was soft and flat, and peristalsis was normal.

Two days after admission the patient had a hemorrhage from the bowel. She became pale and weak, and the blood pressure fell to 66 systolic, 30 diastolic; the heart rate rose to 116. A diagnosis of typhoid fever was made at this time. Bleeding from the bowel occurred several times more during the next two days. The liquid diet was stopped, and she was given only cracked ice for three days. During this time her hemoglobin fell to 64 per cent, and the red cell count to 3,050,000. She was given three transfusions of whole blood and one of plasma, together with other fluids intravenously and by hypodermoclysis.

On admission the patient was given Aureomycin and penicillin. The next day streptomycin was started. Tepid sponge baths were given for the fever. A medical consultant who saw the patient two days after admission agreed with the diagnosis of typhoid fever. Chloromycetin was started at this time, and the Aureomycin, penicillin, and streptomycin were stopped. Chloromycetin was first given in doses of 1250 mg. (five capsules) every three hours; this dose was gradually reduced until she was getting 500 mg. (two capsules) every three hours. Chloromycetin was given for two weeks altogether.

Four blood cultures taken during the first three days of hospitalization came back positive for **S. typhosa.** A blood culture taken five days after admission, when the patient had been taking Chloromycetin for three days, showed no growth. No typhoid organisms were cultured from the stools or urine on repeated examinations.

The temperature returned to normal after five days of Chloromycetin therapy, and the patient was discharged cured after a stay of three weeks in the hospital.

She had no further trouble until March 7, when she came in complaining of nausea and malaise, and appearing slightly jaundiced. Her subsequent course was typical of mild homologous serum hepatitis, which probably resulted from the transfusions of plasma she received while in the hospital. She appears at present to have made a good recovery.

An investigation of possible sources of infection showed that, at the patient's home in the country, she drank spring water or well water and used a privy. There was no history of any cases of typhoid at her home. At her rooming place in town she used town water. The master of the house had had typhoid twenty years ago, and one of his sons had had typhoid as a child. She had visited a friend near Hillsboro on three week-ends prior to becoming ill. She often got fruit for herself at a grocery store in Hillsboro. Her County Board of Health explored all possibilities, and was unable to find a definite source of infection.

The patient had had typhoid vaccine (3 doses) in 1946, and an intradermal "booster" dose in 1947. She had had no typhoid vaccine in 1948 or 1949.

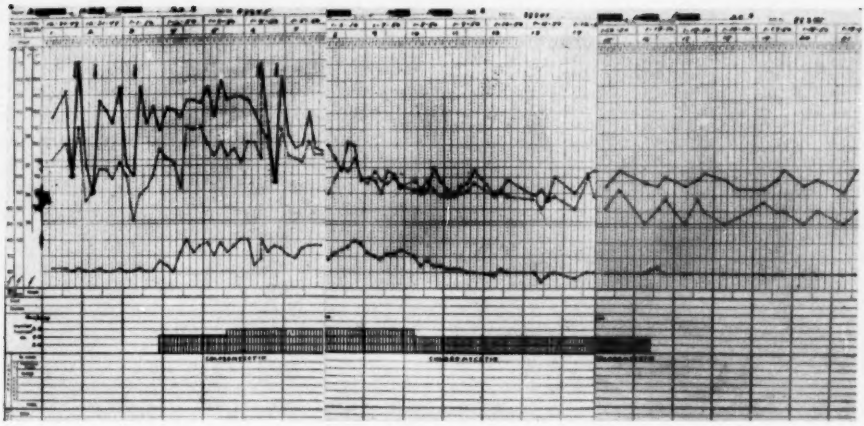

Fig. 1. Response of the patient's temperature to Chloromycetin.

Comment

This patient's fever had the gradual onset that is often seen in typhoid. She had malaise and headache, which are characteristic. There was no history of nosebleed or early diarrhea, though diarrhea developed later, and was thought to be caused by the Aureomycin. She had marked variations in temperature, and frequent chills and sweats. Chills usually occur at the beginning of typhoid; when they occur late, they are often due to some complication. This patient, incidentally, had pyelonephritis.

The typical typhoid temperature rises gradually for several days and then levels off, with moderate daily remissions. It becomes more remittent during the third week, and usually falls by lysis. A sudden fall in temperature between the end of the second week and the beginning of the fourth week suggests the possibility of hemorrhage. Intestinal perforation is the most severe complication, and usually occurs during the height of the disease in the third week. This patient had a rather severe intestinal hemorrhage and had to have three transfusions of blood and one of plasma.

Another common symptom, which was not marked in this patient, is meteorism. This patient had a few typical rose spots, a palpable spleen, a "typhoid tongue," and, after her hemorrhage, rather typical tenderness about the cecum. We were not sure that she had a dicrotic pulse, but her pulse was slow in relation to her temperature—a usual finding in this disease. She did not have the delirium that is often present in severe cases. Leukopenia was present. The positive blood cultures and the positive agglutination tests, of course, confirmed the diagnosis. Treatment with Chloromycetin proved to be remarkably effective in shortening the course of the disease in this patient.

Conclusion

It would seem that we have in Chloromycetin an efficient therapeutic agent for typhoid fever. It is an effective remedy at any stage of the disease[15]. The organism does not become resistant, and the drug is just as effective in the treatment of a relapse as it was originally. It seems, however, that relapses may be avoided if the drug is given in sufficient dosage and over a long enough period.

The typhoid lesions, and especially those found in the Peyer's patches, do not heal rapidly, and for this reason hemorrhage, perforation, and other complications may occur after the patient becomes afebrile.

Chloromycetin seems to be mainly bacteriostatic, though it probably has a mild bactericidal action as well. The drug is remarkably free of toxic or allergic reactions.

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ESOPHAGEAL RESECTION, UPPER THIRD, WITH END-TO-END ANASTOMOSIS

A Case Report

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DURHAM

Since Adams and Phemister[1] reported, in 1938, the first successful transthoracic esophagogastrostomy for carcinoma, esophageal lesions in increasing number have been treated by this technique. As the stomach has been mobilized to higher and higher levels within the chest, this means of re-establishing alimentary continuity has come to be preferred in many cases to the more tedious techniques of dermatoplasty and intestinal shunts.

Recently, attention has focused on the esophagus itself. Experiment and clinical observation have shown that this viscus can be mobilized extensively without embarrassment of blood supply, and that its inherent elasticity will permit reunion after sizable segments are resected. Swenson and Clatworthy[2] described partial resection and re-anastomosis of the esophagus on dogs; 20 out of 26 survived, and no deaths occurred where less than 50 per cent of the esophagus was excised. This report included one clinical case in which a successful re-anastomosis was done after removal of a benign stenosis. Gross[3], in 1948, reported a successful suture of the esophagus following resection of a congenital stricture in an 11 month old boy. In 1949, Parker and Brockington[4] reported that, of 21 dogs subjected to resection of one third of the thoracic esophagus with end-to-end suture, 14 survived, and in only one did a slight stricture develop. Two patients on whom palliative resection for carcinoma was done by the same technique survived long enough to demonstrate the success of the anastomosis; one was able to swallow for three months.

The following case report confirms the observations made above, and suggests a use for this procedure where lesions lie above the aortic arch or even within the neck.

Report of a Case

A Negro woman, aged 54 years, entered Duke Hospital on January 13, 1944, with the complaint of increasing difficulty in swallowing that had begun three months earlier. A lesion causing complete obstruction to the esophagus just below the sternoclavicular junction was demonstrated by roentgenogram (fig. 1) and esophagoscopy. Biopsy was negative, because narrowing was so

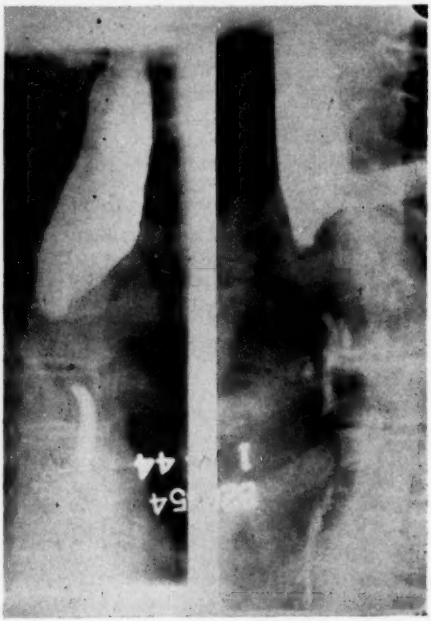

Fig. 1. Preoperative roentgenograms showing complete esophageal obstruction just below the sternoclavicular junction.

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abrupt that a satisfactory specimen could not be taken within the area of stricture.

The absence of pain or palpable metastasis, and the generally good physical condition of the patient favored an operative attempt to remove the obstructing mass.

On January 29, under endotracheal ether and cyclopropane anesthesia, the left side of the chest was entered posteriorly through the bed of the sixth rib. The contents of the left pleural cavity appeared normal. There were no pulmonary adhesions. Hilar and mediastinal glands were palpable, but none were enlarged. The obstructive lesion of the esophagus was not at first visible or palpable. After dividing the mediastinal pleura at the aortic arch, a tape could be passed around normal esophagus and the viscus freed upward to a hard, fusiform mass level with the aortic convexity. The mass was adherent to the aorta, trachea, and left innominate vein. Branches of the bronchial, esophageal, and intercostal arteries were divided and ligated; and by blunt dissection the tumor was freed from the aforementioned structures. Several branches of the vagus nerve were preserved. No cardiac irregularity attended the dissection.

The tumor, which was completely circumscribed, was found to extend into the superior thoracic hiatus and to measure about 4 cm. in length. Removal at such a level could not be accomplished from within the chest; and even had the upper limit of the tumor been accessible, it was, at that time, considered technically impossible to join the esophagus to an abdominal viscus. A Stamm gastrostomy was done and the thorax closed. Convalescence was uneventful.

The obstacles were challenging. If means could be found to bridge a gap approximating 6 cm. in the upper esophagus, we could remove a grossly resectable tumor that would otherwise present a hopeless prognosis. Why could not the esophagus be drawn into the neck, the tumor removed, and reanastomosis performed? Not only would the tumor thus be positively attacked, but anatomic continuity of the esophagus would be re-established.

Could the esophagus be stretched sufficiently to permit this operation? Dissection on fresh cadavers indicated that the relaxed esophagus would bear stretching to one third again its normal length. On the assumption

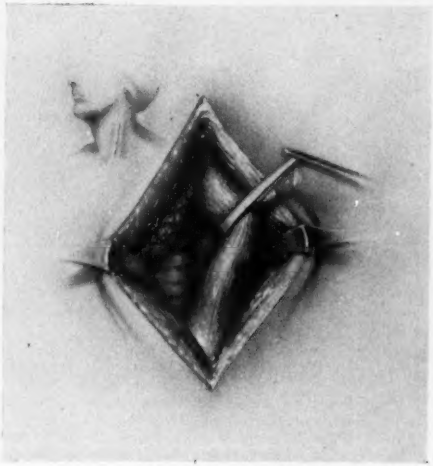

Fig. 2. Transcervical exposure of the esophagus, with the upper limit of the tumor visible at the jugular notch.

that the patient's esophagus was 25 cm. in length, the extreme increment possible would be 8 cm. Sutures would hold without tension if the defect were not greater than 6 cm.

On the basis of this information, it was decided to attempt removal of the tumor through a transcervical incision. If tension or poor blood supply should make anastomosis impossible, the lower stump could be closed and a cervical stoma made with the upper segment. In the meantime, a Lucite tube 10 cm. in length, with internal diameter of 1 cm., was made to be used as a prosthesis should this appear feasible as an alternative procedure.

A second operation was performed on February 12, 1944, a vertical incision being made between the bellies of the left sternocleidomastoid muscle. The inferior thyroid artery and vein were cut and the gland drawn forward. Anterior retraction of the carotid sheath gave ready access to the cervical esophagus, and by digital dissection it was easily freed into the thorax (fig. 2). Induration and fusiform swelling were found 2 cm. below the jugular notch. Since the vessels to the esophagus within the thorax had been sectioned and the lower end of the tumor freed, complete mobilization was quickly attained. In order to prevent local contamination and possible mediastinitis, the area was packed with gauze and the incision was

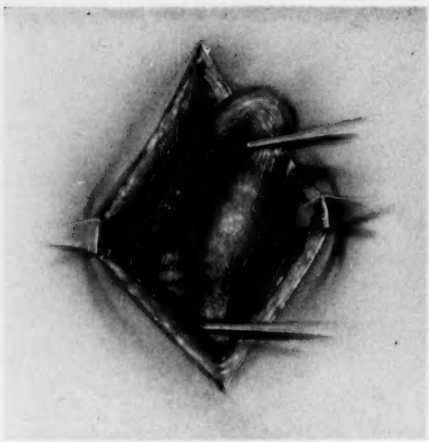

Fig. 3. The tumor exposed by drawing the upper thoracic esophagus into the neck.

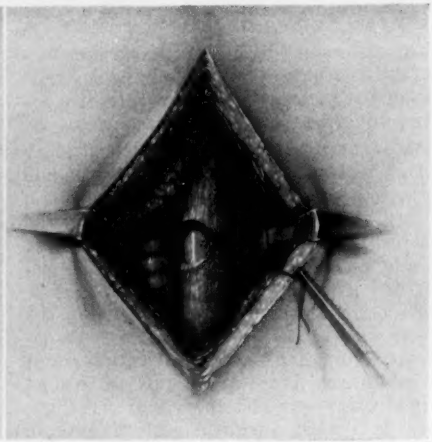

Fig. 4. Anastomosis of the upper thoracic and cervical portions of the esophagus within the neck after removal of the tumor. The Lucite stint is visible in the esophagus.

closed until an inflammatory seal had time to develop. Redundancy of the esophagus, however, made it apparent that subsequent anastomosis could be achieved.

The third operation was done on February 18. The wound was re-opened and the mediastinal gauze pack removed. The tissues around the esophagus were thoroughly sealed.

A snare, threaded with blunt wire, was placed around the esophagus below the tumor. By gentle traction and with surprising ease the tumor was drawn above the jugular notch. The snare was then removed and clamps were applied (fig. 3).

After isolating the field with warm Miculicz pads, stay stutures were placed in the esophagus above and below the lesion to prevent retraction and rotation. The esophagus was divided 1 cm. below and above the tumor, so that the total specimen removed measured 6 cm. in length. The distal segment bled freely. The Lucite tube was inserted as a stint, and was held in place with a suture threaded through two perforations at its center. The ends of the esophagus were then joined with interrupted sutures of no. 70 cotton. As the sutures were brought down, there was a sense of gentle tension, but no tearing or distortion of the tissues (fig. 4). Three grams of crystalline sulfanilamide were dusted into the wound, and the tissues were closed around one Penrose drain.

Liquids in small amounts were given orally after a gastrostomy feeding was regurgitated into the mouth on the third day. A barium swallow on the eighth day entered the stomach, although its passage was slightly delayed at the cardia by what appeared to be tautness of the lower esophagus (fig. 5). A full liquid diet could be taken by the seventeenth day, and four days later the patient could eat a soft diet.

The postoperative course was complicated by intermittent fever from the seventh to the thirty-third day. This fever was believed to be caused by a localized mediastinitis, for a small collection of barium could be detected outside the esophagus at the suture line (fig. 5). Upon removal of the Lucite tube on the thirty-third day the temperature became normal.

Roentgen examination on March 27, thirty-eight days after the third operation (fig. 6), was reported as follows: "There is no delay in the passage of barium and very little, if any, irregularity in the region of the resected carcinoma. The lumen is patent, and no barium is seen to leak out into the mediastinum as on previous examination. Barium enters the stomach much more rapidly. . . . The lower end of the esophagus is still stretched. We cannot be certain of any definite recurrence of tumor. The general impression is that there has been marked improvement and satisfactory re-establishment of lumen."

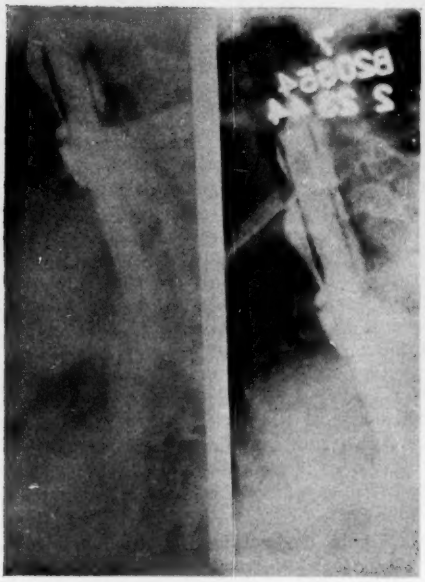

Fig. 5. Roentgenograms taken eight days after operation, showing the Lucite tube in the esophagus. Barium passed readily into the stomach, but there appears to be some extravasation at the site of the anastomosis at the level of the clavicle.

Direct visualization showed a normal lumen at the anastomosis, with complete epithelialization except for one small, granulating area situated posteriorly.

The specimen removed at operation was described by the pathologist as measuring 5 cm. in length. The tumor itself was 3.5 cm. long, annular, cicatrizing, and ulcerated. Microscopically, the lesion was identified as an anaplastic squamous cell carcinoma which had destroyed the mucosa and extended into and through the muscular coat. (Since the tumor had been adherent to the aorta and trachea, invasion had undoubtedly extended to these structures.) Linear extension was not detected.

The patient was discharged forty-five days after the last operation. She returned three weeks later with partial obstruction due to an annular constriction at the anastomosis. Biopsy showed only inflammatory scar tissue. The ability to swallow was restored by dilatation. Within three months obstruction recurred, but since the patient refused further instrumentation we could not know whether it was due to recurrence of the tumor or to inflammatory scarring. She died at home on December 7, 1944, ten months after operation, her physician listing pneumonia as the cause of death. Autopsy was not permitted.

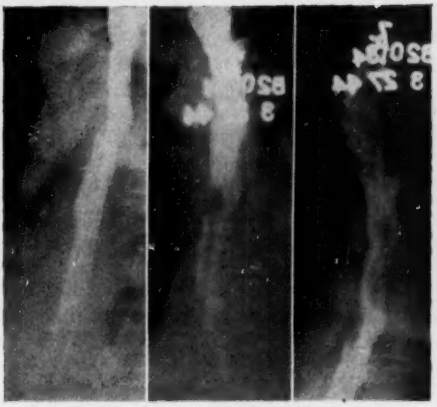

Fig. 6. Roentgenograms taken on the thirty-eighth postoperative day, six days after removal of the Lucite tube. Barium passed readily into the stomach, with no extravasation, irregularity, or constriction at the site of anastomosis.

Comment

In retrospect it is believed that the Lucite tube served no useful purpose in this case, and that the localized mediastinitis might not have occurred had the suture holding the tube not been placed through the line of anastomosis. The early development of stricture has two possible explanations: (1) recurrence of the tumor, since microscopic study of the specimen showed extension of malignant cells beyond the confining limit of the esophageal wall; (2) inflammation and scarring incident to localized infection and delayed healing at the suture line.

Summary and Conclusions

1. After transthoracic mobilization, a segment of superior thoracic esophagus containing carcinoma was removed through the neck, and continuity was restored by end-to-end anastomosis. Deglutition was possible until recurrence of scarring closed the esophagus three months later.

2. Even though the esophagus was extensively mobilized and rejoined within the neck, the blood supply to the lower segment remained good.

3. Esophageal elasticity is ample to permit the removal of a 5 to 6 cm. segment and resuture without undue tension.

4. The use of this technique appears applicable, not only for small or early tumors lying high within the esophagus, but particularly for benign strictures from whatever cause. It has the additional advantage of preserving the cardiac sphincter.

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EXFOLIATIVE DERMATITIS DUE TO PHENOBARBITAL ENDING FATALLY

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Within recent years the use of the barbiturates has reached enormous proportions. These drugs are among the most valuable sedatives available, and undesirable reactions to them are comparatively infrequent. The common reactions are well known, and in most instances their treatment consists merely in discontinuing the drug. Within recent years it has been recognized that dangerous reactions to the barbiturates may occur in an occasional case. So far as we can determine, exfoliative dermatitis is the most severe reaction encountered with the therapeutic use of the barbiturates.

Out of 13 cases of exfoliative dermatitis due to barbiturates reported in the literature since 1936[1], only 4 patients have recovered. Phenobarbital was the principal offender in these 13 cases. On the basis of the clinical data accumulated in these 13 reported cases, we believe that a diagnosis of fatal exfoliative dermatitis due to phenobarbital is justified in the case reported below, despite the lack of sufficient laboratory data and postmortem studies.

Case Report

A 59 year old white woman was admitted to the City Memorial Hospital in Thomasville on April 9, 1949. She was critically ill and complained of vomiting, a rash over her entire body, and fever. She stated that she had always enjoyed good health and had never taken medicine of any kind until about five weeks before admission to the hospital. At that time a sudden severe pain developed in the right upper quadrant, radiating posteriorly to the region of the right scapula. Soon after the onset of the pain she began to have nausea and vomiting. Her family physician was summoned and a diagnosis of gallbladder colic was made. Opiates were given for relief of the pain, and Transentine-Phenobarbital (Transentine 59 mg., phenobarbital 20 mg.) and dietary measures were prescribed. She made a gradual recovery and was asymptomatic at the end of approximately one week.

The same medication was continued, and at the end of two weeks a red, itching, and burning rash appeared on her face and spread rapidly over the entire body. Twenty-four hours after the onset of the rash she began to have nausea and vomiting, but no pain. Her temperature varied between 103 and 104 F. She was seen by her family physician, who ordered her to discontinue the use of phenobarbital. She was given Benadryl (50 mg. every four hours) and a lotion for the skin, and was told to force fluids. Her condition became progressively worse until her admission to the hospital.

Physical examination

Physical examination on admission revealed a critically ill, moderately obese white woman who was extremely restless. The temperature was 104 F., the pulse 120, blood pressure 118 systolic, 70 diastolic. The entire body showed a generalized erythema with marked thickening of the skin and scaling which was most pronounced around the mouth, nose, and ears. There were numerous fissures of the mouth. The conjunctivae were swollen and injected. The mouth and tongue were extremely dry and dirty. There was no enlargement of the lymph nodes, and the nasopharynx was essentially normal. The lungs were clear throughout, and examination of the heart was negative. There was evidence of moderate arteriosclerosis. The abdomen was scaphoid and symmet-

rical, with no tenderness, spasm, or rigidity. Examination of the genitourinary organs revealed nothing of significance. Pelvic and rectal examinations, as well as a neurologic examination, were negative.

Accessory findings

A blood count made on admission showed 3,580,000 red blood cells, a hemoglobin of 73 per cent, a color index of 1.02, and 10,200 white blood cells, with 37 per cent lymphocytes, 4 per cent monocytes, and 59 per cent polymorphonuclears. Repeated blood counts made during her stay in the hospital showed no significant change. The urine had a specific gravity of 1.019 and an acid reaction; it contained albumin (2 plus), 50 white blood cells per high power field, and an occasional hyaline cast. Repeated urinalyses revealed no significant change. Blood culture was negative. The nonprotein nitrogen was 30 mg. per 100 cc. on admission, and one week later had increased to 50 mg. The icterus index on admission was 12 units. The urine was not tested for arsenic or barbiturates.

Course in the hospital

During her two weeks in the hospital, the patient's temperature rarely dropped below 101 F. The exfoliation became much worse and involved the entire body surface, including the scalp, palms, and soles. Vomiting increased progressively, despite various alleviative measures. At the end of the first week of hospitalization the patient was unable to retain anything by mouth. Intravenous fluids were administered daily, and repeated transfusions were given. Penicillin and Benadryl were given throughout her stay in the hospital. Various lotions and oils were applied to the skin without any noticeable results. Despite these therapeutic measures, the patient died on April 22, 1949.

Comment

Clinically, it is impossible to differentiate exfoliative dermatitis due to barbiturates from that due to the arsenical compounds. Barefoot and Callaway[1] have pointed out that conjunctivitis is rare in the latter type of exfoliative dermatitis, but is frequently present in the former. Conjunctivitis was present in our case.

Laboratory methods are not sufficiently reliable to establish a diagnosis of barbiturate poisoning without question. The finding of therapeutic levels of barbiturates in the urine would be of some value, but would not produce conclusive evidence. The period of ingestion of the barbiturate and the size of the dose seem to have no relation to the onset or severity of the clinical manifestations.

From our experience with this case and from a study of the literature, it seems that the best means of establishing a diagnosis in the average case is an adequate history. In view of the widespread use of barbiturates, it would appear that the condition must certainly occur more frequently than is recognized.

From the data available on exfoliative dermatitis due to barbiturates, there seems to be no indication for limiting the use of these drugs. It should be kept in mind, however, that such a reaction may occur. When patients who are receiving barbiturates complain of various skin manifestations, they should receive more than casual attention.

Summary and Conclusions

1. A case of fatal exfoliative dermatitis believed to be due to phenobarbital is reported.

2. Exfoliative dermatitis due to barbiturates is an uncommon but usually fatal reaction.

3. The presence of conjunctivitis associated with exfoliative dermatitis may suggest a barbiturate drug as the causative agent.

4. The most important aid in the diagnosis of exfoliative dermatitis due to barbiturates is a careful history.

5. All patients receiving barbituric acid derivatives who complain of skin symptoms should be observed very closely.

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THUMBNAIL SKETCHES OF EMINENT PHYSICIANS

PHYSICIANS OF NORTH CAROLINA

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DURHAM

THOMAS FANNING WOOD

Thomas Fanning Wood was born in Wilmington, North Carolina, on February 23, 1841. Following the failure of the whale fisheries in Nantucket, Massachusetts, his New England parents had moved to the South and established their home in North Carolina. Thomas grew to be an ambitious young man, and, following his years in high school, he apprenticed himself to various physicians in Wilmington in order to learn medicine. In his spare time he worked in a drug store.

At the beginning of the Civil War he volunteered as a private in the Eighteenth Regiment of the North Carolina infantry, and served at Fort Fisher, North Carolina, and Coosawatchie, South Carolina. After the Seven Days Battles around Richmond in 1862, he was transferred to the North Carolina Hospital in that city and was detailed by the Secretary of War to attend lectures at the Medical College of Virginia, then in session. Wood proved a brilliant student, and in February, 1863, prior to graduation, he was called before the Army Medical Board and was made an assistant surgeon with the rank of captain. Thus began his distinguished army medical career. After assignment to the Third Regiment, North Carolina infantry, Jackson's corps, he served at the Battles of Chancellorsville, Winchester and Gettysburg. He was continuously with the same regiment during Grant's campaign in the Wilderness, and with General Early's army in the campaign from Lynchburg to Washington. His regiment was later transferred to the army around Petersburg in 1864-1865; and Wood was with Lee's army at the surrender on April 9, 1865.

On his return to Wilmington following cessation of hostilities, Wood found a terrible epidemic of smallpox. Organizing a hospital for the care of the sick, he treated over 1300 cases of the disease. It was during these postwar years that Dr. Wood made his greatest contributions to North Carolina medicine, in the field of public health .

Acting on a petition from the North Carolina Medical Society, written by Dr. Thomas Fanning Wood and his associates, the North Carolina State Legislature in 1877 passed the first law creating a State Board of Health. It was a small beginning. The State Medical Society was invested with the powers of a board of health, and an annual appropriation of $100 was made. At the first meeting of the State Medical Society following adjournment of the legislature, Dr. Satchwell of Rocky Point was appointed president of the new Board of Health, and Dr. Wood was named secretary.

There had been a few permanent local health boards in America between 1790 and 1830, chiefly in port towns, for the purpose of administering quarantines. During those years deaths were recorded by the sextons. After 1830, cities and towns began to rely on doctors for birth and death statistics, and by 1860 the majority of American towns had health boards. It was not until ten years later, however, that salaried medical officers were employed[1]. Progress in public health legislation was delayed by the Civil War, and although Lemuel Shattuck's report to the State of Massachusetts recommended a state board as early as 1850, this did not become an actuality until some years later.

There were many signs of retrogression in preventive medicine through all sections of the country, even after the war's termination. In the South the systematic medical service for the poor was abandoned. Arrangements for free vaccination in Mississippi were abolished, and South Carolina gave up the registration of vital statistics[1]. Southern physicians had an almost insurmountable task in dealing with the rapidly rising death rate among Negroes herded into towns, poverty stricken and suffering from tuberculosis and syphilis, and with the poor health of the white population after four years of war. The efforts of some conscientious workers began to show results, and four years after the surrender Massachusetts took the lead in creating the first state board of health. In the next decade eighteen other states emulated this example.

The pioneers in these efforts were to a large extent army physicians who carried their military interests in preventive medicine into civilian life. Dr. Richard Shryock, in his study of the origins of the public health movement, pointed out that army and navy medical service have always afforded

training in preventive medicine.

"It is natural therefore, that these services have contributed much to the development of preventive medicine in the United States, as well as in other nations. It is highly probable that the various young physicians who enlisted in the Civil War, and even afterwards, manifested an active interest in public health, achieved that interest in the service. There were many such, e.g., Dr. S. W. Abbott of Massachusetts, a pioneer American demographer; Dr. T. F. Wood, the founder of the North Carolina State Board of Health; and perhaps most notable of all, Dr. John S. Billings, whose career as a sanitarian and librarian is well known."(1)

In his first report on the progress of the newly established Board of Health, to the North Carolina Medical Society in Goldsboro on May 15, 1878, Dr. Wood said:

"I am satisfied that nothing but a sincere desire to make a beginning in the great work of sanitary reform and to put the ball in motion could have induced this body to have accepted such a great work with such trifling means."(2)

He never relaxed his efforts, and in 1879, on his recommendation, the legislature made improvements in the public health laws. Following that session, the first permanent organization of the Board was effected in the old "McAdoo House" in Greensboro on May 21, 1879, during a meeting of the State Medical Society. Dr. Wood was chosen secretary for a term of six years. In the following year the appropriation for the Public Health Board was increased from $100 to $200. In 1881 the State Medical Society honored Dr. Wood by electing him its president*; but he was becoming pessimistic about the future of preventive medicine in North Carolina. The appropriations were still negligible, and his attempt to have a comprehensive vital statistics law enacted met with failure. His discouragement was reflected in his statement that "The interest and objects of the board seem to be in a retrograde condition in North Carolina, while the opposite condition is true of other states."(2)

His unselfish zeal bore fruit, however, and in 1885 the public health laws were amended, making county boards more efficient, allowing a printing fund not to exceed $250, and increasing the general appropriation of the Board from $200 to $2000 per year. At last the state board was on firm ground, and Dr. Wood's vision was becoming a reality.

Thomas Wood received an honorary M.D. degree from the University of Maryland in 1868, and in 1888 the University of North Carolina conferred on him an honorary LL.D. He was a founder of the American Public Health Association and was its first vice president. He served on the Board of Medical Examiners of North Carolina; and in 1878, with M. J. DeRosset, began the *North Carolina Medical Journal*, of which he was the editor-in-chief until his death. Because of his interest in vital statistics, he edited a monthly periodical, the *Bulletin of the North Carolina Board of Health*. He was an enthusiastic botanist and an authority on the flora of his state. This knowledge made him a valuable member of the Committee for the revision of the Pharmacopeia for the periods 1880-1890 and 1890-1900. In 1887 his catalogue, written in collaboration with Gerald McCarthy on the botany of his section of the South, was published as a part of the Elisha Mitchell Scientific Society of the University of North Carolina, under the title of "Wilmington Flora." At one time he proposed to reissue Dr. Curtis' "Woody Plants of North Carolina," adding sections of his own; but ill health prevented the accomplishment of this project.

Despite a serious cardiac ailment, he continued to edit the state journal and prescribe for patients from his bed. Throughout his life he maintained an active interest in the affairs of his home community, and he was president of the Wilmington Library Association when he died on August 22, 1892, at the age of 50.

Dr. Richard H. Lewis, who succeeded Dr. Wood as secretary of the State Board of Health, said: "The State Board of Health owes its origin to the enlightened mind and benevolent heart of the late deeply lamented Dr. T. F. Wood of Wilmington."

It is clear that Thomas Fanning Wood, of the late nineteenth century, would have been in accord with the statement made in 1949 by Dr. James B. Conant in his introduction to "Public Health in the World Today":

". . . it is clear that if we are to attain the social objectives of making the new knowledge equally effective in the lives of all the people of a nation—let alone of the entire world—improving our methods of curing disease is not enough. The problem today is keeping well."(3)

M. B. T.

* Twenty-eight years later his son, Edward Jenner Wood, famous for his studies of pellagra and sprue, was elected first vice president of the society.

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HEALTH INVENTORY—BY MACHINE?

The political re-education which physicians are undergoing has taught many to keep an ear to the ground and to watch for straws in the wind. Washington newspaper columnists are often the first to give hints on the trends of thought and the long range plans of the bureaucrats. Unfortunately, especially where medicine is concerned, bureaucratic thinking in terms of "the greatest good for the greatest number" often loses sight of first principles.

The very favorable public reaction to large scale roentgen screening for tuberculosis has led people concerned with public health to explore the possibility of adapting the mass technique to other diseases. One columnist reports on the favorable response to a pilot clinic through which 400 to 500 persons a day already have passed. The early detection of incipient stages of disease is a highly laudable goal, but the possibility of attaining it by this technique deserves critical scrutiny.

It is well recognized that incipient tuberculosis can best be diagnosed with the roentgenogram. By the time the disease is detectable on physical examination, it is already in a moderately advanced stage. Such is not the case with the much more frequent diseases which are assuming increasing prominence as the population ages. The separate clinics for the detection, by the simplest and quickest methods, of cancer, diabetes, cardiovascular disease, and mental illness which have been established in many communities are designed to see the greatest number of people in the shortest possible time. They attempt to utilize the well known tendency of American industry to substitute a machine for a man wherever possible, in order to achieve mass production.

The proposal is now made to combine these separate clinics into one glorified medical production line — a "multiphasic screening center"— under the presumption that the individual physician cannot or will not undertake the task. The patient would present himself for his "periodic health inventory" or "complete physical check-up." If the tuberculosis mass survey technique is followed, he might enter one end of a group of trailer trucks, in which technicians would perform a serologic test for syphilis, a roentgenogram of the chest, an electrocardiogram, a blood sugar determination, and a urine examination. The blood pressure could be taken by a nurse. The physician would presumably follow the cancer screening technique, examining the mouth, skin, nodes, rectum, prostate, or breast and pelvis (a vaginal smear done by a technician could be included); he might also listen to the heart. The patient, having been suitably impressed with this display of mechanical devices and laboratory tests, would then be dismissed to be "referred to a physician for prompt treatment."

The only catch in this scheme is that the most important essentials to a dependable evaluation of the health of the individual have been omitted. He has not had either a history or a satisfactory physical examination. Heart disease, for instance, is detected earliest by the *history*—not by the roentgen shadow or electrocardiogram, which are altered in more advanced disease. Cancer of the stomach, one of the most common forms of malignancy, can be suspected only from the history, and can be detected earliest by

a radiologist using time-consuming fluoroscopic examinations. We still do not have available a dependable blood test for screening cases of cancer.

It seems impossible to convince people that the individual doctor-patient relationship is not merely a sacred fetish handed down from antiquity to which all physicians bow in reverence, but that it is the best method developed in 3000 years for giving good personal medical care. The history—when taken by a physician, not checked on a quiz sheet by the patient—is still the most important factor in the diagnosis of disease. Many studies have shown that at least 75 per cent of diagnoses are made correctly on the basis of the history. No method has been or can be devised which will allow any reasonable number of physicians to take histories on 400 to 500 people daily.

The public should not be deluded into believing that examination by machine can exclude or detect all incipient disease. The highly specialized diagnostic detection clinics are looking for only one pathologic process. Regardless of how many are combined into a "multiphasic screening center," the vital ingredient in diagnosis is the physician, who will collect essential data and who in the end must treat the patient. Even the most rabid proponents of such schemes recognize that they are "most beneficial to the public when they are geared to the diagnostic and treatment facilities of the community."[1] The family doctor is the keystone of diagnosis and treatment in the community, and he alone has the opportunity to interpret the symptoms, signs, and laboratory findings in the light of the home environment of the patient. Let us continue to urge the public to seek good medical care regularly, but let us also emphasize that the essential factor is the physician and not the machine.

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THE SENATORIAL PRIMARY

The victory of Willis Smith in the second Democratic primary was an emphatic protest of North Carolina voters against the Truman administration and many of the things it stands for. For that reason it gave satisfaction to many who do not want our country to follow England into Socialism. This satisfaction, however, is tinged with regret that a man who is as generally loved and respected as Frank Graham had to become a casualty in the great game of politics. No doubt many who voted against him did so because they sincerely felt that it was their most effective way to protest against the ruthless methods of the so-called "Fair Dealers" in Washington. Such people did not love Frank Graham less, but their country more.

It is not disparaging Willis Smith, who is destined to make his mark in Washington, to say that many who voted for him knew little about him except that he had pledged to stand firm against further encroachments upon the rights of the people by a power-mad federal government.

John Temple Graves, in his column for June 28, expressed the feeling of many when he said:

"Some of us who cheered without reservation the defeat of Claude Pepper have no cheers as Frank Graham goes down, even though knowing it for the best. There are only tears that a true-hearted gentleman and idealist had to be dragged into and through politics, and, even more, that in the sorry game he was forced to positions which seemed to hedge on ideals for which we honored him even if we could not accept them."

HOSPITAL VISITORS

The weekly broadcasts over station WPTF by Mr. William H. Richardson, of the State Board of Health, are always interesting and full of useful information. One of the most timely of these was based upon an article in the *Health Bulletin* for September, entitled "Hospital Visiting Creates Serious Problems." It is to be hoped that both the address and the article in the *Bulletin* received the widest possible publicity, for "uncontrolled visiting has become a serious menace to the proper treatment . . . of our patients."

Only one who has been a hospital patient can appreciate the harm that can be done by injudicious visiting. It might almost be said that the most important rule for visiting the sick is the famous advice given by Punch to those about to marry: "Don't!" For those who *must* visit hospitals regularly, however, the advice given in the *Bulletin* is excellent. Such an article does far more to help sick people than most attempts to contribute to the medical education of the public.

MEDICAL WOMEN OF NORTH CAROLINA

Beginning with the issue for October, 1949, the *Medical Woman's Journal* has been publishing, in a section entitled "History of Women in Medicine," a series of sketches devoted to medical women of North Carolina. The editor is Dr. Irma Henderson-Smathers of Asheville, who in her own right deserves a place of honor among the medical women of the state.

Thus far, twenty-seven sketches have appeared. This series very appropriately began with Dr. Elizabeth Blackwell, the first woman doctor in the United States. Dr. Blackwell started her medical studies in Asheville, under the guidance of two brothers, Dr. John Dickson and Dr. S. H. Dickson. Dr. John Dickson had been educated both in medicine and in the ministry. He was pastor of the Asheville Presbyterian Church from 1843 to 1845, but before that he had opened and directed a school in which Miss Blackwell taught music and French. Dr. John Dickson's brother, Dr. S. H. Dickson of Charleston, spent his summers in Asheville, and apparently both brothers helped her "read medicine" preparatory to entering the Medical College of Geneva, New York, on November 8, 1847.

The first woman doctor admitted to membership in the State Medical Society—Dr. Susan Dimock of Washington, North Carolina—never practiced in the state. She was graduated from the University of Zurich, Switzerland, and was made a member of the Medical Society of the State of North Carolina in 1872, while she was still abroad. She then became resident physician at the New England Hospital in Boston, where she organized the first school of nursing in the United States. A ship in which she sailed for England in 1875 was wrecked, and she was drowned when only 28 years old. In admitting Dr. Dimock to membership, North Carolina became one of the first four states to recognize women doctors. Massachusetts led by admitting a woman in 1869; Kansas, Iowa and North Carolina each admitted one in 1872.

The first woman doctor who actually practiced in North Carolina was Dr. Annie Lowrie Alexander. She was born in Mecklenburg County and graduated at the head of her class from the Woman's Medical College of Pennsylvania in 1884. In 1885 she made the highest average before the State Board. She practiced in Charlotte until her death in 1929, and was highly respected for her ability and personality.

Dr. Clara Ernull Jones, the wife of a doctor and the mother of two doctors, began the study of medicine in 1890, when she was 43 years old. After she had practiced a short time in Goldsboro with her husband and oldest son, she was made resident physician in charge of the women's wards in the State Hospital for the Negro Insane in Goldsboro. She held this post for twenty-six years, until she retired at the age of 75. One of the buildings in the institution was named in her honor.

Another prominent medical woman of North Carolina was Dr. Anna M. Gove, who, as physician to the Woman's College of the University of North Carolina from 1893 to 1937, was known and loved by hundreds of college students.

One of the most brilliant members of a brilliant family was Dr. Delia Dixon Carroll, who was physician to Meredith College from its opening in 1899 until her death in 1934. She also did private practice and had a devoted following.

Other North Carolina medical women of note include Dr. Catherine Hayden, superintendent of St. Agnes Hospital in Raleigh from 1904 to 1915; Dr. May S. Miles, who is physician to the Greensboro Y.W.C.A. and to the girl students of Guilford College; Dr. Alice Johnson of Aberdeen, who was professor of psychiatry at the Woman's Medical College of Pennsylvania from 1923 to 1938; Dr. Mary Lapham, a pioneer in the use of artificial pneumothorax in tuberculosis; and Dr. Mary Martin Sloop, who with her husband, Dr. Eustace H. Sloop, has been instrumental in building and maintaining a school at Crossnore which has enabled hundreds of boys and girls to obtain an education. The Woman's College in 1943 conferred upon her the honorary degree of Doctor of Laws.

Dr. Henderson-Smathers is to be commended for the excellent work she has done in preparing these sketches of North Carolina's medical women.

Clinicopathologic Conference

Bowman Gray School of Medicine of Wake Forest College

A 31 year old white man was admitted to the North Carolina Baptist Hospital on January 19, 1950, stating that his urine had been scanty and dark for thirty-six hours.

On the day preceding admission he had noted the sudden onset of oliguria associated with lethargy, nausea, diarrhea (five very dark brown, watery stools), anorexia, vomiting (twice), and a very dark brown color to his urine. He had taken no medicine recently, except some pills three weeks prior to admission for vague low back pain. A week later he had had an upper respiratory infection lasting seven to eight days. Three days prior to admission he noticed puffiness about his eyes. He had had no known exposure to toxic substances and no recent transfusions. There had been no chills, fever, or pain. He denied any melena, weight loss, abdominal pain, or alcoholism, but stated that he had noted a gradual increase in the size of his abdomen over a three year period.

During World War II the patient had served in New Guinea and in the Philippines, and had been given suppressive doses of Atabrine. In the spring of 1946, following his discharge from service and the cessation of Atabrine, he began to have recurrent bouts of fever, chilly sensations, and discomfort in the left upper quadrant. These occurred about every six months and lasted several days. The patient was treated with various anti-malarial drugs, although parasites were never demonstrated on repeated examinations. The last episode—in June, 1949—was associated with jaundice for the first time. He entered a Veterans Administration Hospital, where jaundice, splenomegaly and impaired liver function were noted, and a diagnosis of chronic infectious hepatitis was made.

On admission there, his white cell count was 2100, with 5 per cent eosinophils; the sedimentation rate was 26. Serologic tests for syphilis were negative. There was increased urine urobilinogen (no bile). Total serum proteins were 7.5 Gm. per 100 cc.—3.3 Gm. of albumin and 4.2 of globulin. The serum bilirubin was 6.2 mg. per 100 cc., and a cephalin flocculation test gave a 2 plus reaction. Febrile agglutination tests, a complement fixation test for amebiasis, and a bone marrow examination were negative. A chest film showed slight elevation and flattening of the right diaphragm. Abdominal roentgen studies and intravenous pyelograms were negative. At the time of discharge the patient was improved.

Physical examination: On admission here, the temperature was 99 F., the pulse 90, respiration 18, blood pressure 114 systolic, 64 diastolic. The patient was pale but oriented and only slightly uncomfortable. No jaundice, petechiae, or glandular enlargement was noted. There was minimal edema of the soft tissues of the orbit, but no other edema. The heart and lungs were normal. A firm, smooth, rounded, non-tender mass was felt in the left upper quadrant; it extended 6 to 8 cm. below the left costal margin, which did not move with respiration. The liver was felt 1 to 2 cm. below the right costal margin, and was firm, smooth, and non-tender. There was no tenderness in the costovertebral angles, and neurologic examination was not remarkable.

Accessory clinical findings: The hemoglobin was 11.5 Gm., red cell count 4,700,000, white cell count 4,450, with 62 per cent segmented polymorphonuclears, 28 per cent nonsegmented polymorphonuclears, 1 per cent eosinophils, 5 per cent lymphocytes, and 4 per cent monocytes. Toxic granulation of the polymorphonuclear cells was noted. Urinalysis revealed a specific gravity of 1.048, a 4 plus reaction for albumin, and innumerable white cells, red cells, and granular casts. The nonprotein nitrogen was 51 mg. per 100 cc., fasting blood sugar 100 mg., total serum protein 6.5 Gm., with 3.5 Gm. of albumin and 3.0 Gm. of globulin. The carbon dioxide combining power of the blood was 41 vol. per cent, calcium 9.8 mg. per 100 cc., phosphorus 5.1 mg., bilirubin 2.0 mg., chlorides 552 mg. Two stool examinations revealed no blood, ova or parasites, and on culture no pathogens were seen. Serum cholesterol was 247 mg. per 100 cc., alkaline phosphatase 1 unit. The heterophile agglutination test was postive in a dilution of 1:28; cold agglutinins were present in a 1:40 dilution.

Electrocardiograms on three occasions showed no evidence of myocardial disease.

Course in the hospital: The patient was placed on a "rice diet," and fluids were limited to 1000 cc. daily. During the first few days he did not appear to be in any great distress, and remained afebrile. The urinary

output varied between 200 and 800 cc. for several days, then gradually increased during his hospital stay. Urinalysis on almost all occasions revealed albumin (3-4 plus), many red blood cells, and occasional granular casts. Cultures subsequently showed coliform bacilli, and the patient was given streptomycin.

On the fourth day fluoroscopic examination revealed a pleural effusion on the right. On thoracentesis 80 cc. of straw-colored fluid was obtained, with a specific gravity of 1.008 and 8 to 10 red blood cells per cubic millimeter. Culture was negative, and no acid-fast bacilli were found. The pathology department found no abnormal cells in the fluid.

The serum chlorides remained above 80 milli-equivalents per liter with the administration of normal and hypertonic saline. The carbon dioxide combining power dropped on several occasions to around 40 volumes per cent, and the patient was given sixth molar lactate. The nonprotein nitrogen rose gradually, reaching 203 mg. per 100 cc. by the twelfth day, and remaining above 200 during his stay. The blood pressure was low initially, but during the latter half of his hospital stay it ranged between 150 and 180 systolic, 70 and 90 diastolic. The eyegrounds were unchanged.

Culture of the bone marrow revealed two colonies of a gram-negative, non-lactose fermenter (alcaligenes). Three blood cultures were negative and a culture from the throat contained predominantly alpha streptococci and staphylococci. Darkfield examination of the urine and blood revealed no leptospirae.

Seven days after admission, fluoroscopic examination showed increased pleural effusion, and 1400 cc. of fluid was obtained by thoracentesis; culture of this was sterile. Because subphrenic abscess was suspected, surgical consultation was obtained. On the fifteenth hospital day, an exploratory operation was done on the abdomen and right subphrenic space. Ascites was noted, and the liver was found to be nodular. On that day, the patient had a chill and his temperature rose to 102.8 F. Chloromycetin and penicillin were begun, and methionine, liver extract, choline and hypertonic glucose solution were added to the treatment. Oxygen was administered, and a high calorie, high protein formula was given by stomach tube.

His hemoglobin dropped to 8 Gm. during the first postoperative week, and he was given two transfusions of packed red blood cells. He became gradually worse, and began to vomit bright red blood. Ascites re-appeared, and 1400 cc. of sanguineous fluid was removed by paracentesis. During the final week there was no appreciable change in the total serum protein or albumin-globulin ratio. The leukocyte count rose, and ranged between 14,000 and 25,700; the total lymphocyte count was never greater than 2 per cent. The prothrombin time remained slightly elevated, but never exceeded 18.4 seconds, against a control of 12.8 seconds. The serum bilirubin did not exceed 3.3 mg. per 100 cc.

One week after operation the patient complained of pain in the chest and dyspnea, which was relieved by oyxgen. The urinary output during the last three days dropped appreciably. The day before death, the temperature rose to 102 F., and vomiting subsided. The following day, the patient complained of severe abdominal pain not relieved by Demerol and codeine. He was given 150 mg. of Etamon intravenously over a fifteen minute period; his pain was relieved promptly, but the blood pressure fell to 85 systolic, 60 diastolic. The blood pressure failed to rise during the next hour, and a transfusion was started. The pulse became accelerated and heart sounds were barely audible. Respirations ceased and the heart stopped beating, despite intravenous Adrenalin, on the twenty-seventh hospital day.

Clinical Discussion

DR. DAVID CAYER: I believe that the emphasis can be placed more properly in this case if the past history is given before the present illness. In summary, the patient was a 31 year old white man who served in New Guinea and the Philippines for a period of approximately four years, and apparently was in good health. Shortly after his discharge from the service, he discontinued his atabrine and began to have attacks of fever, chilly sensations, and discomfort in the left upper quadrant. These recurred approximately every six months, lasted several days, and apparently subsided following antimalarial therapy, even though parasites were not found. This history is not uncommon in service men who have returned from malarial areas, and is entirely compatible with the clinical diagnosis of recurring malaria.

He noted some increase in the size of his

abdomen over a three year period. In the absence of more specific information, I would be inclined to attribute this to gradul enlargement of the spleen. In July of 1949 he became jaundiced for the first time, and was hospitalized at a VA hospital. Here he was found to have jaundice, splenomegaly, impairment of liver function, and leukopenia; a diagnosis of chronic infectious hepatitis was made. Roentgen examination of the gastro-intestinal tract and gallbladder, and intravenous pyelograms were negative. Since we have no history of urinary complaints at that time, it is difficult to understand why an intravenous pyelogram was done, unless there was some question as to whether the mass in the left upper quadrant might have been kidney rather than spleen. In any event, the patient was discharged as improved. Improvement might have been due to the four month period of hospitalization and bed rest alone.

For three months following discharge he remained well enough to work and was relatively asymptomatic until his admission to this hospital. This was occasioned by an acute illness which followed an upper respiratory infection and was characterized by periorbital edema, oliguria, nausea, vomiting, and dark urine. The striking absence of fever, chills, pain, or weight loss throughout the remainder of his hospital stay is of extreme importance in the differential diagnosis.

The pertinent laboratory data revealed a mild anemia, an initial leukopenia (although the white cell count rose terminally to 25,700, with a lymphopenia), and the persistent presence in the urine of large quantities of albumin, white cells, red cells, and granular casts. The patient's course was marked by recurring acidosis, the development of ascites, a pleural effusion, progressive retention of urinary nitrogen, and failure to respond to antibiotics. Exploration of the right sub-diaphragmatic space revealed a nodular liver.

The possibility of tumor is suggested by the gross appearance of the liver, the presence of ascites and pleural effusion, the negative blood cultures, the absence of fever, and the failure to respond to antibiotics. Against such a diagnosis, however, is the absence of a primary tumor site. Thorough roentgen examinations made within the past three months had revealed no abnormality in the gastrointestinal tract or gallbladder. The enlargement of the left kidney noted on the roentgenogram of the abdomen was symmetrical, and therefore not suggestive of tumor. If the pulmonary findings were due to a primary renal tumor, we would also expect to find nodular densities in the lungs, and pain. Such a diagnosis would not account for the splenomegaly previously noted; furthermore, progressive and rapid renal failure is usually not associated with tumors of the kidney.

The presence of both chronic and acute infectious processes is suggested by the splenomegaly, the initial leukopenia, the patient's age, the absence of abnormal cells and blood in the fluid removed from the abdomen and thorax, the history of an upper respiratory infection preceding the final episode, and the negative roentgen survey prior to his admission.

If the physical findings and laboratory data obtained from the VA hospital can be relied upon, we are safe in assuming that the patient had liver disease, since hepatomegaly, splenomegaly, leukopenia, jaundice, impairment of the liver function tests, and spider angiomas were noted. The problem presented is chiefly that of correlating this diagnosis with the final picture of diffuse, severe, parenchymatous renal disease.

There are many conditions which will produce degeneration of the renal epithelium as well as liver disease. We surmise from the history that the patient had malaria. This could account for the enlarged liver and spleen and the leukopenia, but the absence of fever would be difficult to explain. Blackwater fever, which is a rare and serious complication of malaria and may occur after multiple attacks of malaria, is also associated with chills, fever, and evidence of hemolysis, which this patient did not have.

Weil's disease, or infection due to *Leptospira icterohaemorrhagiae*, usually has an abrupt onset characterized by chills, fever, nausea, vomiting, pain, purpura, and jaundice. Often a history of exposure to rats or fleas can be obtained. The complete lack of systemic reaction and the unsuccessful attempt to demonstrate the spirochete in the urine and blood of this patient would be against such a diagnosis.

If we are correct in assuming that this patient had been ill for three or four years, the possibility of amyloid disease must be considered, particularly in view of the en-

largement of the spleen and left kidney, and the marked albuminuria. Classically, amyloidosis follows chronic debilitating febrile diseases such as tuberculosis and osteomyelitis, although it may be primary. In the latter form, it is apt to involve unusual sites such as the tongue or striated muscle, but it has been found even in association with malignancies. Patients with amyloid disease, however, usually have polyuria, and renal insufficiency is rare. When oliguria does occur, the urine is of low specific gravity, whereas the specific gravity of this patient's urine was persistently high.

There is an unusual complication of hepatic necrosis and hepatitis which has been given many names, such as "cholemic" nephrosis or "hepatonephritis." This disorder usually occurs in patients who have previously been asymptomatic; it comes on suddenly, and is frequently associated with enlargement of the liver and spleen and the rapid onset of oliguria, albuminuria, and nitrogen retention. Such patients at postmortem examination are found to have marked degeneration and necrosis of the tubular epithelium, which is thought to be due to a toxin elaborated in the diseased liver.

The presence of red cells in the urine of the patient under discussion, the rapid fall in hemoglobin, and the high specific gravity of the urine are more suggestive that the renal involvement was predominantly glomerular. All of the urinary findings can be adequately explained by the diagnosis of acute glomerulonephritis, since we have a history of an upper respiratory infection, followed, after a latent period, by periorbital edema, dark urine, nausea, vomiting, oliguria, albuminuria, and cylindruria. This diagnosis might also account for the enlargement of the kidney seen on the roentgenogram. Often such patients remain afebrile. The absence of eyeground changes or a previous history of urinary disease, and the negative pyelograms are against the possibility of chronic nephritis or polycystic kidney disease. It would seem, then, that the findings in this case are best explained by multiple diganoses.

Dr. Cayer's Diagnoses

1. Postnecrotic cirrhosis.
2. Acute glomerulonephritis.

Anatomic Discussion

DR. THOMAS N. LIDE: At autopsy the body was well developed and well nourished. Icterus was marked. A healing operative wound 13 cm. in length was found in the right flank, and two healing suprapubic wounds, each closed by a single black silk suture, represented the sites of paracenteses. Ecchymosis surrounded these wounds and extended downward over the symphysis to involve the scrotum and shaft of the penis. There was moderate sacral and ankle edema.

Nineteen hundred cubic centimeters of cloudy fluid having a foul odor was found in the peritoneal cavity. A moderate fibrinous exudate was present over the surface of the bowel and was particularly marked in the lower half of the abdomen; it was associated with hyperemia, mainly around the cecum, and involving the omentum and mesentery. The colon was dilated and filled with gas.

The right pleural cavity contained 1400 cc. of straw-colored fluid, and the left 200 cc. There was about 150 cc. of similar fluid in the pericardial cavity. A few sub-epicardial hemorrhages were found in the right auricle and left ventricle, and petechiae were seen on the mitral and tricuspid valves. The heart showed no changes, and was not enlarged. The trachea and major bronchi were hyperemic and edematous. The right and left lower lobes were partly collapsed and dark red in color. The lungs otherwise showed no gross change. Petechiae found near the cardia were the only changes noted in the esophagus; these petechiae were also present in the gastric mucosa.

The liver weighed 1560 Gm., and was grossly nodular and irregularly scarred. Several large yellowish nodules replaced the left lobe, which was connected to the right by a flattened belt of collapsed hepatic stroma. The nodules varied from 1 to 4 cm. in diameter, the majority being approximately 2 cm. in diameter. They were present throughout the entire extent of the liver and were separated by dense, firm, fibrous tissue in which blood vessels of medium size could be seen. There was no evidence of extrahepatic biliary obstruction, though the gallbladder was distended with dark green bile. No changes were found in the bile ducts. The pancreas weighed 155 Gm., and was more friable and edematous than usual. The spleen was tremendously enlarged, weighing 865 Gm. It was firm, with a mottled, grayish-red surface, and relatively little bulging above the cut surface.

The kidneys were much enlarged, weigh-

ing together 710 Gm., as compared to a normal of approximately 300 Gm. They were about equal in size, and were pale and more or less mottled; numerous tiny petechiae were evident when the capsule was stripped away. There was some bulging above the cut surface of the capsule and an undue prominence of the cortical markings. In general the cut surface of the kidneys appeared somewhat glassy and opaque. The pelves and calices were thin, without grossly evident lesions. No changes were found in either ureter or in the bladder. The prostate was small. The testes weighed 35 Gm. together, as compared to a normal of 40 to 50 Gm.

The microscopic changes centered about the liver and kidneys. The mass of nodules in the liver were found to represent regenerating liver tissue. The arrangement in the individual lobules was irregular, and central veins were lacking in the majority of the lobules. No fatty infiltration or degeneration was evident. Several small foci of coagulative necrosis were seen in the left lobe, where the most marked change was found. These probably resulted, not from hepatitis, but from embarrassment of the hepatic circulation due to distortion of the vessels by the large nodules. There was a marked inflammatory reaction throughout the portal spaces, with compression between the lobules. Proliferation of small bile ducts was moderate, but no bile thrombi were found in any of these small ducts.

The spleen was to a great extent replaced by fibrous tissue, which was more marked along the sinusoids, but was present throughout the pulp, forming a prominent reticular network in the sections stained by Masson's trichrome method. Lymphoid replacement was prominent, and no proliferation of the reticulo-endothelial cells was found. We were unable to find actual platelet phagocytosis to account for the patient's hemorrhagic tendency, which was most likely secondary to prothrombin deficiency.

There was marked interstitial pancreatitis with edema, but no changes were noted in the pancreatic glandular structures. The periadrenal adipose tissue was the site of a similar chronic inflammatory reaction, consisting mainly of lymphocytes and mononuclear phagocytes without polymorphonuclear cells. The surface of the bowel, mainly the colon, was covered by fibrinous exudate with inflammatory cells similar to those described in the periadrenal tissues. The testes showed a marked reduction in activity, without spermatogenesis.

In the kidneys a most interesting lesion was found, consisting mainly of endothelial proliferation of the glomerular tufts, which were practically bloodless throughout both kidneys. Numerous tubules were filled with fresh blood and with albuminous material, but we were not able to demonstrate the actual site of the bleeding, though it was probably the glomeruli. It is of much interest that the tubules showed no cloudy swelling or degeneration, and that they did not contain bile casts or other evidences of nephrosis such as one often finds in association with severe hepatitis. The lesions were those described by Bell and called by him acute proliferative glomerulonephritis. They represented the type of lesion found occasionally in association with streptococcic infections, or with other acute or chronic infectious diseases.

In considering this patient's course, we believe that his hepatitis began prior to the acute episode ten months before death, and probably was responsible for the episodes of chills, fever, and malaise which he had had from time to time during a four year period. Jaundice appeared only after the development of extensive cellular injury ten months before his death. Lucke[15,16] has reported cases of hepatitis with survival periods of approximately two years, and Kunkel and Labby[17] have reported one case in which the patient was still living after six years, though with symptoms of severe portal obstruction. It has been stated by Kunkel and Labby[17], and by others, that once hepatic insufficiency with portal obstruction begins in post-necrotic cirrhosis, the course is usually progressive without remission. Post-necrotic cirrhosis differs in this respect from portal cirrhosis, with its therapeutic remissions.

The changes in the liver of this patient were typical of those occurring after severe hepatitis, with large irregular nodules and deep scars. The liver is apparently not affected equally throughout its entire extent by the injurious agent, but is damaged more or less segmentally. The deep scars probably do not represent true fibrous tissue proliferation, but rather a collapse of the stroma following complete necrosis and autolysis of the parenchymal cells. The hepatic tissue present in this patient's liver at the time of death was almost entirely new tissue following regeneration from partly destroyed lobules.

The ascites is usually considered to be indicative of portal obstruction, as is the fibrosis of the spleen. The peritonitis present at autopsy may well have resulted from the paracentesis, although in other cases of hepatitis peritonitis has developed without drainage of abdominal fluid. The lesions found in the cecum, consisting mainly of severe edema with inflammatory changes and hyperemia, are common in cases of portal obstruction.

It is generally considered that ascites occurs secondary to portal obstruction, particularly if there is also a reduction in the serum protein. Recent experiments at the Mayo Clinic[2] have indicated that the outpouring of lymph is the major source of the ascitic fluid in dogs with portal obstruction. When a cellophane band was placed around the portal vein, a slowly developing obstruction occurred, but ascites did not develop unless plasma proteins were also reduced by plasmapheresis. When the cellophane band was placed around the inferior vena cava in the thorax, a slowly developing occlusion, with massive ascites, occurred in a period of about three weeks. Concomitantly the plasma proteins fell. It was demonstrated in these dogs that, with the first evidence of hepatovenous congestion, hepatic lymph flow increased and reached a figure, in cannulated animals, of approximately twenty times the normal. The ascitic fluid in these animals was high in protein content, and corresponded more closely with that found in the hepatic lymph from the same dogs, and with the ascitic fluid of patients with hepatic portal obstruction, than it did with the thin fluid, low in protein content, found after ligation of the portal vein itself.

I do not believe that the lesions in the kidneys can be attributed to the cirrhosis, inasmuch as these lesions differ from those often found in severe hepatic insufficiency. The history of a moderately severe upper respiratory infection occurring about two weeks before the development of oliguria suggests the onset of an acute nephritis independent of the hepatitis.

Atrophy of the testes was another interesting feature of this case. It has been described previously in cases of hepatitis by numerous investigators[3], who generally attribute this change, as well as gynecomastia, to the inability of the liver to inactivate estrogens. This patient had no gynecomastia, but his testes were atrophic and inactive.

This case represents another of the various types of morphologic change occurring in the liver following hepatitis. This irregular, scarred, nodular liver is apparently the most common type of terminal lesion in chronic hepatitis, but there can occasionally occur cases which resemble, morphologically at least, Laennec's cirrhosis. A case of the latter type was discussed at this conference last August[4].

Anatomic Diagnoses

1. History of infectious hepatitis (by clinical findings)
2. *Post-necrotic cirrhosis of the liver with portal obstruction*
3. Intense icterus
4. Ascites, with a history of multiple paracenteses
5. Generalized peritonitis
6. Pericardial and bilateral pleural effusions
7. Acute diffuse proliferative glomerulonephritis
8. Chronic interstitial pancreatitis
9. Atrophy of the testicular tubules.

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2. Volwiler, W., Bollman, J., and Grindlay, J. H.: A Comparison of Two Types of Experimental Ascites, Proc. Staff Meet., Mayo Clin. 25:31-33 (Jan. 18) 1950.
3. Rather, L. J.: Hepatic Cirrhosis and Testicular Atrophy, Arch. Int. Med. 80:397-402 (Sept.) 1947.
4. Clinicopathologic Conference, Bowman Gray School of Medicine of Wake Forest College, North Carolina M. J. 11:145-151 (March) 1950.

Doctor, when you peruse the advertising pages in our journal, remember this: all ads are carefully screened—the items, services, and messages presented are committee-accepted. Our standards are of the highest. The advertisers like our journal—that's why they selected it for use in their promotional program. They seek your patronage and your response encourages continued use of our publication. In turn, the advertisers' patronage helps us to produce a journal that is second to none in our state. When you send inquiries, tell them that you read their advertisement in the **North Carolina Medical Journal.**

There are two aspects to the educational problem (in tuberculosis). First, the getting of knowledge, which is not, after all, a very difficult thing to do . . . We perhaps are sometimes embarrassed by the knowledge we have. The knowledge which we have of tuberculosis is really enormous . . . The second aspect is the difficult problem: making this knowledge effective . . . There are three to educate, the public, the profession, and the patient.—William Osler, M.D., Nat. Tuberc. A. Tr., 1905.

Committees and Organizations

RURAL HEALTH COMMITTEE*

PROGRESS IN THE RURAL HEALTH PROGRAM OF THE MEDICAL SOCIETY OF THE STATE OF NORTH CAROLINA

The North Carolina Rural Health Council Program was started in 1947, under the sponsorship of the Rural Health Committee of the State Medical Society. Much difficulty was encountered by the Rural Health Committee in deciding on a method of approach in developing such a broad program. It was the aim of the committee in the beginning to follow pretty closely the plan advocated by the American Medical Association for organizing Rural Health Councils. This plan is to organize first a State Health Council, composed of representatives from all the organizations in the state which are interested in health matters. Among these are the farm organizations, civic clubs, parent-teacher associations, home demonstration groups, and many others, including of course the State Medical Society, State Health Department, and other allied organizations.

Since the North Carolina Good Health Association was still active following the completion of the Medical Care Program, this organization was asked to be one of the co-sponsors of the rural health program. The Association agreed to this proposal, and rendered valuable aid during the first year of the program. It was through the action of the joint committee that funds were secured from the General Education Foundation with which to finance the first year of the program. Since the funds to carry on the work of the Good Health Association were inadequate during 1949, and since the General Education Foundation failed to provide funds for the second year, the State Medical Society decided to finance the program, and to continue actively to develop it.

In 1949 a State Health Council was set up, and on June 14 and 15, 1950, a third State Rural Health Conference was held jointly with the first annual State Health Council Conference in Raleigh. This conference was well attended, and an extremely interesting and helpful program was presented. It is felt by the Committee on Rural Health that the new State Health Council will be of tremendous help in coordinating the programs of the different health organizations in the state. The cooperation of the State Health Council will be needed in the continued program of the Rural Health Committee in organizing rural health councils. It is expected that through this cooperation the rural health program will receive great impetus.

Before initiating the program for the organization of rural health councils in the different counties of the state, the Rural Health Committee decided that two conditions needed to be met. First, it would be necessary to obtain the service of a field worker who had been trained in health and organizational work. Second, it would be necessary to organize councils in two or three counties in the east, and the same number in the west to get experience and, if possible, form patterns for the organization of subsequent councils. The committee was very fortunate in obtaining Miss Charlotte Rickman, a health educator who was at that time employed by the Illinois State Medical Society as consultant and director in the organization of rural health councils.

The method used for organizing rural health councils in the different counties was as follows: The chairman or some member of the Rural Health Committee met with the local county medical society, with representatives from the county health department, and with the health educator where one was available, to talk over the plan of organization, the possible programs, and the feasibility of organizing a council in the county. If the decision was in the affirmative, Miss Rickman went into the county. Meeting with members of the different organizations of the county and representatives from the different communities, she discussed possible programs that might be of benefit, drew up a list of guiding principles, and arranged programs for meeting the needs of the different communities. The idea was to work with the local citizens—not to plan for them—and to stimulate interest and thought on health matters at the grass roots.

The response in each county has been remarkable, and the cooperation of the differ-

* Members of the Rural Health Committee are J. Street Brewer, M.D., Chairman, Roseboro; Reece Berryhill, M.D., Chapel Hill; Charles L. Harris, Jr., M.D., Williamston; W. P. Richardson, M.D., Chapel Hill; George Bond, M.D., Bat Cave; H. B. Perry, Jr., M.D., Boone; Fred C. Hubbard, M.D., North Wilkesboro; Miss Charlotte Rickman, M.S.P.H., Health Educator, Consultant to the Committee; Mr. James T. Barnes, Executive Secretary, Medical Society of the State of North Carolina, *ex officio* member.

ent health agencies in the program has been stimulating. Of course the ground for such a program had already been pretty well prepared by the State Board of Health through its county health units. It was felt, however, that programs handed down from a national and state level are not enough, because in many instances people seem to resent such an approach, and cannot see how they apply to their individual counties. They seem to need the motivation furnished by individual community thought and planning and cooperation in order to recapture the traditional democratic spirit in solving their own problems.

The committee, of course, recognizes the fact that social and economic conditions in most rural communities have a direct bearing on medical service. Poor roads, poor schools, isolated churches, and other related conditions are responsible for the fact that rural communities have lagged far behind the average urban area in medical and hospital service.

The first rural health council was organized in Alexander County in October, 1948. Representatives from local organizations and communities got together, listed their major county health problems, adopted a set of guiding principles, arranged their programs, and went to work. The first project was the completion of the hospital program in Alexander County. In this, the council rendered valuable assistance. Such programs as "Health Career" days in the schools, Blue Cross Insurance campaigns, health centers, and the organization of a school health committee were set in motion. The need for cooperation among all individuals and organizations interested in health matters was recognized early. The cooperation of the doctors and the Health Department in all the programs was complete.

The second health council was organized in Watauga County in 1949. Chairmen from thirty-six Watauga County communities were appointed, and met to discuss their problems. The local medical fraternity, Health Department, and health educator rendered valuable assistance in organizing the council. The cooperation of the Farm Bureau was secured, and it assisted in the promotion of numerous mass meetings throughout the county. Physicians, home agents, health educators, Farm Bureau officers, and others attended these meetings, and discussed with the members of the local communities such important matters as swamp clearance, garbage disposal, stream pollution, health clinics, unsanitary water supplies, and nutrition. As a result of the survey made by the individual communities a brochure was prepared, listing their resources and problems. The information contained in this brochure pointed indisputably to the need for a "grass roots" approach to the health problems of the county.

Caldwell County became interested in a health council plan in 1949, and asked Miss Rickman to help them. They decided on a broader program, and a much slower approach to the organization of their health council. After three large mass meetings, to which representatives of various organizations were invited, they decided to organize a Community Council which would not only help to solve their health problems, but would answer the need for coordinated action in all the phases of community life. A steering committee, along with representatives of the Medical Society and health educators, decided on an educational plan which they felt would be the best and most democratic approach to their health problems. It was through recommendations of the steering committee, the County Board of Health, and the County Commissioners, that they were able to employ a full-time health educator to supervise the health program in Caldwell County.

We have now moved into the eastern part of the state, and Miss Rickman, with the help of the local physicians and health departments, is busy organizing councils in Wayne and Halifax Counties. The response and cooperation of the medical fraternities and of the health departments have been great. Other counties are interested, and we feel that the movement to organize rural health councils is gaining momentum.

The Medical Society of the State of North Carolina has dedicated itself to the proposition that to rural North Carolina shall come better and more adequate medical care. The Rural Health Committee feels that better health is everybody's business, and that the medical profession has no monopoly on it. The profession does not wish to project itself into the rural health program too far, nor to try to run the show. The rural health program is a sincere and honest effort on the part of the medical profession to stimulate and to help direct the thinking of the rural

people into channels which will make it possible for them to solve the many problems relative to improved health conditions in their own tradition and democratic way. Thus far, results of our efforts have been very gratifying, and the prospects of a worthwhile movement are bright.

BULLETIN BOARD

New Hanover County Medical Symposium

The fourth annual medical symposium sponsored by the New Hanover County Medical Society will be held on August 25 at the Lumina Pavilion, Wrightsville Beach. The program will start at 10 a. m. The speakers and their subjects are as follows:

Dr. Samuel Marshall, Lahey Clinic, Boston—"Diagnosis and Treatment of Tumors of the Neck."

Dr. T. Grier Miller, University of Pennsylvania Hospital, Philadelphia, Pa.—"Disturbances of the Digestive Tract from the Viewpoint of the General Practitioner."

Dr. Emil Novak, Baltimore, Md.—"Indications and Limitations of Endocrine Therapy in Gynecology."

Dr. Chevalier L. Jackson, Philadelphia, Pa.—"Recent Advances in Laryngology and Broncho-Oesophagology."

Dr. Arnold Bargen, Mayo Clinic, Rochester, Minn.—"Present Day Management of Some Forms of Ulcerative Colitis."

All doctors are invited to attend and bring their wives. The local medical auxiliary is planning a noon-day "Dutch" luncheon for the women, and at 6:30 p. m. the ladies are invited to accompany their husbands to the cocktail hour, followed by a barbecue dinner given by the New Hanover County Medical Society. Reservations should be made at once. The following hotels and cottages have agreed to give preference to members attending the meeting:

Ocean Terrace Hotel, Kitty Hotel, Landis Cottage, Hanover Cottage, Ocean Inn.

News Notes from the North Carolina Tuberculosis Association

Dr. Herman F. Easom, medical director of the Eastern North Carolina Sanatorium at Wilson, was elected president of the North Carolina Tuberculosis Association at the annual meeting held in Durham May 22 and 23. Dr. M. D. Bonner of Jamestown, Dr. R. B. C. Franklin of Mt. Airy, and Dr. A. L. Ormond of Hickory are members of the executive committee.

Dr. M. D. Bonner, superintendent and medical director of the Guilford County Tuberculosis Sanatorium, was elected president of the North Carolina Trudeau Society at its annual meeting in Durham on May 22. Other officers elected were Dr. C. G. Milham of Hamlet, vice president, and Dr. Hege Kapp of Forsyth County, secretary-treasurer.

The group voted to amend the constitution of the society to make eligible for membership any physician practicing in North Carolina who is interested in chest diseases.

* * *

Miss Anne Mann, field secretary of the North Carolina Tuberculosis Association for the past four years, will leave to become associate in seal sale with the National Tuberculosis Association on August 1.

* * *

Among those re-elected to the board of directors of the North Carolina Tuberculosis Association in May were Dr. M. D. Bonner of Jamestown, Dr. N. Thomas Ennett of Beaufort, Dr. R. B. C. Franklin of Mount Airy, Dr. J. H. McNeill of North Wilkesboro, Dr. Paul Ringer of Asheville, and Dr. Hillis L. Seay of Huntersville.

New directors-at-large include Dr. S. B. McPheeters of Goldsboro, Dr. Lynwood Williams of Kinston, Dr. W. A. Anthony of Gastonia, Dr. G. G. Dixon of Ayden, and Dr. G. G. Oleen of Monroe.

News Notes from the Bowman Gray School of Medicine of Wake Forest College

Forty-one M.D. degrees and two M.S. degrees were awarded by the Bowman Gray School of Medicine in commencement exercises held at Wake Forest on June 5. The Weinstein Award of $50 was made to Dr. Charlotte Rita Kay of Charlotte. The prize is given each year by Dr. Weinstein of New Orleans, Louisiana, for the best paper by a senior student on a subject connected with obstetrics and gynecology. Dr. William Thaddeus Bethea, Jr., of Dillon, S. C., received the Shepardon Award of $25. The award, given by Mrs. David Cayer in honor of her father, is based on scholarship, responsibility, consideration of patients, and promise of continuing in its highest ideals the practice and art of medicine.

* * *

A grant of $3,000 has been made by the Ciba Pharmaceutical Company to Dr. J. Maxwell Little, professor of pharmacology, for study on the results of various drugs. Dr. Little will collaborate with Dr. James F. Donnelly and Dr. Richard L. Burt of the department of obstetrics and gynecology in studies on the effect of vasodilator drugs on toxemias of pregnancy.

* * *

Dr. Weston M. Kelsey has been promoted from the position of assistant professor of pediatrics to that of associate professor. Other recent appointments include the following: Dr. Robert L. Tuttle and Dr. William R. Vance, instructors in microbiology and immunology; Dr. John B. Reinhart, instructor in pediatrics; Lucius A. Moore, Jr., assistant in preventive medicine; Miss Lucille Kessler, assistant in clinical psychology; Miss Mary C. Sumner, associate in psychiatric social work; A. Hooker Goodwin, director of audio-visual aids; Dr. Edward B. Truitt, Jr., instructor in pharmacology; Dr. Jerry Aikawa, instructor in internal medicine; Dr. Henry L. Valk, instructor in internal medicine; Dr. C. Glenn Sawyer, instructor in internal medicine and associate in physiology; and Miss Marietta Crowder, assistant in biochemistry.

New assistants in clinical medicine are Dr. Kenneth Cheek of High Point, Drs. Marvin E. McRae and Taylor Brooks of Greensboro, Dr. Benjamin Vatz, and Drs. A. J. Crutchfield and Hege Kapp of Winston-Salem.

* * *

Dr. Robert B. Lawson, professor of pediatrics, will speak on the subject of "Coxsackie Virus" at one of the sessions of the International Congress on Pediatrics, meeting in Zurich, Switzerland, July 24 to 28.

News Notes from the Duke University School of Medicine

Dr. John T. Cuttino, associate in pathology, has been appointed acting dean of the School of Medicine of the Medical College of the State of South Carolina in Charleston.

The 37 year old Duke pathologist, who will also hold the position of associate professor of pathology, assumed his duties on July 1.

News Notes from the State Board of Health

During the first quarter of 1950, 247 North Carolinians died as the result of automobile accidents. Deaths from accidents other than those associated with motor vehicles during the first quarter of 1950 totalled 291.

The State Board of Health is creating a unit designed to make a study of preventable accidents, with a view to doing what it can to help educate the people against those practices which result in the needless crippling and death of others.

State Board of Medical Examiners

The North Carolina State Board of Medical Examiners will meet at the Sir Walter Hotel in Raleigh on Monday, September 25, for the purpose of interviewing applicants for licensure by comity.

American College of Surgeons

Color television of surgical procedures from Massachusetts General Hospital to an auditorium in Mechanics Hall is one of the features planned for the thirty-sixth Clinical Congress of the American College of Surgeons, which will be held in Boston from October 23 to 27. Twenty-four hospitals in Boston and vicinity will hold operative clinics for the visiting surgeons during the week. Official meetings, scientific sessions, medical motion pictures, a large technical exhibit, and the twenty-ninth annual Hospital Standardization Conference are among the other features of the extensive program, which is expected to attract around five thousand surgeons and hospital representatives from the United States, Canada, and other countries. Hotel headquarters will be at The Statler and Copley Plaza.

International College of Surgeons

The International College of Surgeons, United States Chapter, will hold its fifteenth Annual Assembly and Convocation in Cleveland, Ohio, October 31, November 1, 2, 3, 1950.

All doctors of medicine interested in surgery and its advancement are invited to attend, and can obtain a program upon request to Arnold S. Jackson, M.D., Secretary, Jackson Clinic, Madison 4, Wisconsin. For hotel reservations, write the Committee on Hotels, International College of Surgeons, U. S. Chapter, 511 Terminal Bldg., Cleveland 13, Ohio.

Medico-Military Symposium, Fourth Naval District

To keep military Reserve Medical Officers of the armed forces—Army, Navy and Air Force—posted on the latest developments in the field of medical science, a Medico-Military Symposium for officers of the Fourth Naval District will be held at the U. S. Naval Hospital in Philadelphia from October 23 to 28.

All members of the medical profession are cordially invited to attend.

The National Society for Crippled Children and Adults

The Annual Convention of the National Society for Crippled Children and Adults will be held October 26, 27 and 28 at the Stevens Hotel in Chicago.

Mississippi Valley Medical Society and American Medical Writers' Association

The fifteenth annual meeting of the Mississippi Valley Medical Society will be held at the Elks Club in Springfield, Illinois, September 27, 28, and 29. More than thirty clinical teachers from the leading medical schools will conduct this great postgraduate assembly, whose entire program is planned to appeal to general practitioners. NO REGISTRATION FEE will be charged, and every ethical physician is cordially invited to attend.

The American Medical Writers' Association will hold its annual meeting at the Elks Club on September 27. Programs of both meetings may be obtained from Harold Swanberg, M.D., Secretary, M.V.M. Society and A.M.W. Association, 209-224 W.C.U. Bldg., Quincy, Ill.

Commission on Chronic Illness

The Commission on Chronic Illness is the first national agency to be charged with the responsibility for studying the integration of programs of the many health and social agencies working in this field. The various forms of chronic illness in this first unified approach include heart disease, cancer, tuberculosis, hardening of the arteries, apoplexy, diabetes, arthritis and rheumatism, various types of paralysis, as well as chronic disabilities resulting from disease or accident.

These conditions have common problems and require integrated programs in addition to the single disease approach with which the public is familiar. This requires coordinated community action.

Dr. Morton L. Levin is Director of the Commission, which is an organization of thirty persons prominent in medicine, industry, education, government, and business. Founded by the American Medical Association, American Public Health Association, American Public Welfare Association and American Hospital Association, it is also supported financially by the American Medical Association, American Cancer Society, American Heart Association, the National Society for Crippled Children and Adults and the New York Foundation.

Its technical staff, with national headquarters at 535 N. Dearborn in Chicago, will study the need for and stimulate or perform further administrative research in the field of chronic illness and plan a national campaign to acquaint the public with the positive aspects of chronic illness. Finally as a result of information gathered, there should result a set of programs for continued, concerted action by local, state and national agencies.

Blue Cross Commission

Nearly a hundred million dollars, representing more than 88 per cent of income, was paid to hospitals by the voluntary, non-profit Blue Cross Plans for care of members during the first quarter of 1950.

From a total income of $109,801,301, the 90 Blue Cross Plans of the United States and Canada paid $96,989,972 for members' care and used only $9,184,564 (8.37 per cent) for operating expenses.

There are more than 38,000,000 persons enrolled in the Blue Cross Plans in the United States and Canada, representing more than 24 per cent of the United States population and 21 per cent of the Canadian people.

American Heart Association

Acting to help meet the urgent need for qualified research workers who can concentrate their full time in the heart disease field, the American Heart Association is establishing Career Investigatorships as part of its research program, according to an announcement made by Dr. H. M. Marvin, president of the Association.

Dr. Marvin explained that nominations for Career Investigators may be made by members of the Scientific Council of the American Heart Association, deans of medical schools, and heads of research units in the United States. The nominations should be sent to Dr. Charles A. R. Connor, the Association's Medical Director.

The Career Investigator will engage in research of his own choosing in the cardiovascular field. He may work in any institution in the United States which offers adequate facilities, and he will be free from additional administrative duties at that institution. Not more than 15 per cent of his time is to be spent in teaching. Certain Career Investigators may have access to patients, but any income thus created will be considered part of the stipend provided by the American Heart Association.

The Mary M. Roberts Fellowship

The Board of Directors of the **American Journal of Nursing** Company announces the establishment of the Mary M. Roberts Fellowship, a competitive fellowship, the purpose of which is "to assist a qualified professional nurse to prepare herself in the technical aspects of writing about nursing and nursing education for professional and lay publications."

The criteria for making the award will be the general professional qualifications of the candidate and her interest and facility in writing. One of the requirements for candidacy will be a specially prepared manuscript on some subject pertaining to nursing. The award will provide a sum of $2,500 to $4,000, the exact amount to be determined by the Award Committee, for one academic year of study in a college or university. The award will be made in the late summer.

Nurses who wish to qualify for this award may get the necessary application blank by writing immediately to "Fellowship," American Journal of Nursing, 1790 Broadway, New York 19, N. Y.

Plastic Surgery Award

The Foundation of the American Society of Plastic and Reconstructive Surgery offers as its 1950 award $500.00 (first prize of $300.00, second prize of $200.00) and a certificate of merit, for essays on some **original unpublished subject in plastic surgery.**

Competition shall be limited to residents in plastic surgery of recognized hospitals and to plastic surgeons who have been in such specific practice for not more than five years.

The first prize essay will appear on the program of the forthcoming annual meeting of the American Society of Plastic and Reconstructive Surgery, to be held in Mexico City, November 27-29, 1950. Essays must be in before August 15, 1950.

For full particulars write the Secretary, Dr. Clarence R. Straatsma, 66 East 79th Street, New York, N. Y.

CARE

There are an estimated 300,000 cases of tuberculosis in the Philippines. Yet there are only 1,500 hospital beds for TB victims—1,000 of them at Quezon Institute, on the outskirts of Manila.

Quezon Institute is doing its best to help as many victims as possible in the fight against the white plague. In addition to its 1,000 bed-ridden patients, the sanitarium provides clinic care for 300 ambulatory cases. But lack of the most basic supplies—food, clothing, linens, and even up-to-date books on modern medicine's methods of attacking the disease—combine to hinder seriously the institution's program.

The supplies it needs in its fight against TB can be sent by Americans through CARE, 20 Broad St., New York City, or any local CARE office. Ten dollars will provide a CARE package of food, with the nourishing items so essential to tubercular care, or a household linen package containing the sheets, pillowcases, towels that are a necessary part of hospital supplies. Five-fifty will send a cotton textile package to provide dresses and suits for TB patients. A contribution in any amount to the CARE-UNESCO Book Fund will send the latest and best American books on tuberculosis to bring the Institute's staff up-to-date on medical techniques.

Present Health Conditions in Israel

The appearance of Volume 1, 1950, of **The Hebrew Medical Journal** (Harofe Haivri), inaugurates the twenty-third year of its publication under the editorship of Moses Einhorn, M.D.

Written in Hebrew, with English summaries, the journal is a contribution to improving the health of the new State of Israel, aiding as it does the development of Hebrew medical literature, and thus the newly established Hebrew University - Hadassah Medical School.

In the current number, a symposium is presented on various phases of disease and health in Israel.

For more information write to **The Hebrew Medical Journal,** 983 Park Avenue, New York 28, N. Y.

(BULLETIN BOARD CONTINUED ON PAGE 372)

Classified Advertisements

FOR SALE

Well established general practice in Goldsboro, N. C. Grossed $21,000.00 last year. If obstetrics is added it will do much more. Equipment available at once includes a five-room office conveniently located down-town, x-ray-fluoroscope, diathermy, infra-red, ultra-violet, inter-com system, cordiette furniture, bookkeeping supplies, etc. A new 100-bed addition to the local hospital is now being built. Leaving to specialize. Write B. I. Tart, Jr., M.D., Goldsboro, N. C.

LOST

While attending State Medical Convention—one small sunburst pin. Center small diamond surrounded by small pearls. Finder please notify Mrs. Alfred A. Kent, Jr., Granite Falls, N. C.

AUXILIARY

A MESSAGE FROM THE PRESIDENT

I started my year with an overwhelming feeling of inadequacy; then the thought crept in: Of course I am inadequate, because I am only one. With all of you to support me, though, much can be done!

It is a temptation when summer comes to relax and forget that we have any duties. That would be perfect if all opposition relaxed too. All of the communications which come to us from the A.M.A. offices and from our own public relations office in Raleigh make us aware that we have much to do—not as doctors' wives or members of the Auxiliary, but as citizens.

Oliver Wendell Holmes is credited with saying, "The important thing is not so much where we stand, but in what direction are we moving?" There is no question about where we stand—but are we content just to stand, or are we moving in the proper channels?

You are key women in your communities; what you do and say has a great deal of influence. Let us accept our places with a conscience that will not let us relax.

The Medical Society is placing more responsibility in our hands than it ever has before. We have already been asked to help secure resolutions against any form of compulsory insurance or any system of socialized medicine. Your local auxiliary president has received information regarding this. It is very important that we work at this assignment diligently. North Carolina is too near the bottom of the list of states sending in resolutions. It is something which certainly will not require much effort on our part during these summer months, but which can show unbelievable results if we give it the necessary attention. I am sure the doctors can count on us.

Medical Economics last year called the Auxiliary a "slightly erratic aid in medicine's camp." I hope that this arouses your ire as it did mine. On the other hand, Dr. Edward Bortz said of us that the Auxiliary represents probably the most effective instrument the medical profession has in the field of public relations, but a most neglected one. In North Carolina we are not being neglected—so I am asking all of you to do what you can to justify the kind statements Dr. Bortz made of us. He is not alone in his opinion of our worth. The doctors are realizing more and more what concrete help we can give. I am sure we shall fulfill their expectations.

I hope that all of you are having pleasant experiences this summer; but please—not complete relaxation! Remember, "IT'S YOUR CRUSADE TOO." Incidentally, has your Auxiliary studied that most worthwhile pamphlet?

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BOOK REVIEWS

Textbook of Endocrinology. Edited by Robert H. Williams, M.D., Executive Officer and Professor of Medicine, University of Washington Medical School, Seattle. With the collaboration of Peter H. Forsham, Harry B. Friedgood, John Eager Howard, Edwin J. Kepler, William Locke, L. Harry Newburgh, Edward C. Reifenstein, Jr., William W. Scott, George Van S. Smith, George W. Thorn, Lawson Wilkins. 793 pages with 168 figures. Price, $10.00. Philadelphia and London: W. B. Saunders Company, 1950.

The editor has chosen twelve contributors for this volume. All are authorities in their field, not only because of their clinical experience but also because of their intimate contact with basic and clinical investigations.

Chapters are devoted to the pituitary, thyroid, adrenals, testes, ovaries, pancreas, and parathyroids. Of unusual interest are the chapters dealing with the general principles of endocrinology, the influence of endocrines upon growth and development, neuroendocrine and psychodynamic aspects of the endocrinopathies, obesity, and diagnostic laboratory procedures.

The main objective of the text has been well realized—that is, to provide a condensed discussion of the management of clinical endocrinopathies based upon the application of fundamental information obtained from chemical and clinical investigations. This volume can be throughly endorsed as a comprehensive survey of endocrinology.

Methods in Medical Research. Volume 2. Edited by Julius H. Comroe, Jr. Price, $6.50. 361 pages. Chicago: The Year Book Publishers, Inc., 1950.

This series of books is devoted to a description of techniques and methods for investigations in medical research. The current volume discusses methods of study of bacterial viruses, pulmonary function tests, and assay of hormonal secretions. Each section contains a number of short articles by different authors on specific points, such as sterilization of vials, stop cocks and tubing used in pulmonary function tests; bronchospirometry; measurement of gas volumes; and measurement of the velocity of respired gases.

This book will be of interest to those in charge of clinical research programs in the larger hospitals. The techniques are often not adaptable to office practice or to the clinical laboratories in small hospitals.

Clinical Pathology—Application and Interpretation. By Benjamin B. Wells, M.D., Ph. D., Professor of Medicine, University of Arkansas School of Medicine, Little Rock, Arkansas. Price, $6.00. 397 pages. Philadelphia: W. B. Saunders Company, 1950.

This volume is an attempt to bridge the gap between the practice of clinical pathology in the laboratory and the bedside care of patients. The author takes up by systems various diseases, discussing the laboratory procedures which may be helpful in handling the patient. No techniques are given. An attempt is made to indicate when the test should be used and how it should be interpreted.

The terminology applied to the nomenclature of bacteria is not always consistent; no single accepted system appears to have been followed. Discussions of the newer antibiotics such as Aureomycin and chloramphenicol are omitted. The Evans Blue technique for determination of blood volume is discussed; this is certainly not a procedure for routine use, since the drug is still under the control of the Food and Drug Administration. Some simple useful procedures such as the slow relaxation and tendon reflexes in myxedema, the alterations in the eosinophil count in Addison's disease, and the simple digestion of emulsion on x-ray films as a test of pancreatic function are omitted. One reference is usually given for each section at the bottom of the page.

The author has attempted to cover a tremendous field in a book which seems too small to fulfill its purpose.

Handbook of Medical Management. By Milton Chatton, M.D., Instructor in Medicine, University of California Medical School; Sheldon Margen, M.D., Clinical Instructor in Medicine and Research Associate in Medicine, University of California Medical School; Henry D. Brainerd, M.D., Assistant Clinical Professor of Medicine and Pediatrics, University of California Medical School; Assistant Clinical Professor of Pediatrics, Stanford University School of Medicine. Price, $3.00. 476 pages. Palo Alto, California: University Medical Publishers, 1949.

This pocket sized book includes a surprising amount of data. The discussion is arranged in chapters, with a unique method of thumb-indexing by the use of black printed blocks at the edge of the page. The code numbers from the "Standard Nomenclature of Disease" have been included as an aid in the coding of records. Diseases are discussed briefly from the standpoint of diagnosis. Treatment is outlined separately under such headings as emergency treatment, maintenance, management, prophylaxis. Dosages of medications are given in detail. Many helpful practical suggestions for the office management of patients in private practice are given; an example is the card to be carried by a diabetic.

The book should be of especial interest to medical students, house officers, and young physicians entering general practice.

Current Therapy 1950 — Latest Approved Methods of Treatment for the Practicing Physician. Edited by Howard F. Conn, M.D. Consulting Editors: M. Edward Davis, Vincent J. Derbes, Garfield G. Duncan, Hugh J. Jewett, William J. Kerr, Perrin H. Long, H. Houston Merritt, Paul A. O'Leary, Walter L. Palmer, Hobart A. Reimann, Cyrus C. Sturgis, Robert H. Williams. 736 pages. Price $10.00. Philadelphia and London: W. B. Saunders Company, 1950.

The second volume in this series continues the arrangement of the 1949 volume. An impressive array of contributors has been collected, each of whom describes in detail the method of treatment he uses. Where alternative or optional methods may be accepted, another author has described that treatment. As in the previous volume, discussions of the clinical aspects, differential diagnosis, and laboratory diagnostic tests are omitted. Where laboratory tests are specifically indicated in the control of therapy, they are often mentioned. Prescriptions and diet lists are often given in detail. No illustrations or references are included.

A new section on diseases of the locomotor system has been added, and the articles on infectious diseases have been brought up to date. Symptomatic treatment and specific therapeutic measures are separated. The continued use of incomplete sentences and telegraphic style in some sections is distracting. In many instances the pharmaceutical manufacturer distributing a given drug is mentioned, though distinction is not always clearly made between the generic and the trade name of the drug. In some sections it is not clearly indicated when patients should be hospitalized and when they may safely be treated in the home.

The book is an excellent one which should be very helpful to practicing physicians. The editor has been unduly modest in not identifying himself as well as his consultants and contributors have been identified.

Sexual Deviations. By Louis S. London, M.D., and Frank S. Caprio, M.D. 702 pages. Price, $10.00. Washington: The Linacre Press, Inc., 1950.

This book is an attempt to explain deviations from the usual heterosexual pattern. The authors discuss the deviations from a normal sexual goal and attempt to explain through a psychopathologic approach the range of abnormalities and the conditions under which they may occur. The major portion of the book is taken up with the presentation of case histories illustrating the psychodynamics of sexual deviations in such conditions as homosexuality, incest, exhibitionism, sadism, and numerous other aberrations. The case histories seem to be unnecessarily detailed, but this is the psychoanalytic technique.

The question of what constitutes normal psychosexual development and what constitutes a deviation is in need of much more intensive investigation. Apparently so-called sexual deviations are much more widespread than is generally recognized. The unconscious forces producing such deviations should be within reach of psychiatric therapeutic measures.

BULLETIN BOARD

(CONTINUED FROM PAGE 369)

FEDERAL SECURITY AGENCY

Announcement of Regular Corps Examination For Medical Officers, United States Public Health Service

A competitive examination for appointment of Medical Officers in the Regular Corps of the United States Public Health Service will be held on October 9, 10, and 11, 1950. Examinations will be held at a number of points throughout the United States, located as centrally as possible in relation to the homes of candidates. Applications must be received no later than September 11, 1950.

The Regular Corps is a commissioned officer corps composed of members of various medical and scientific professions, appointed in appropriate categories such as medicine, dentistry, nursing, engineering, pharmacy, etc.

Appointments will be made in the grades of Assistant Surgeon (equivalent to Army rank of First Lieutenant) and Senior Assistant Surgeon (equivalent to Captain). In making assignments, consideration is given to the officer's preference, ability, and experience; however, all commissioned officers are subject to change of station and assignment as necessitated by the needs of the Service. Appointments are permanent in nature and provide opportunities to qualified physicians for a life career in clinical medicine, research, and public health. Applicants who successfully complete this examination may ordinarily expect appointment as soon as they become eligible.

Application forms and additional information may be obtained by writing to the Surgeon General, United States Public Health Service, Federal Security Agency, Washington 25, D. C. Attention: Division of Commissioned Officers.

* * *

The opening of a new laboratory for research involving radioisotopes at the National Institutes of Health of the Public Health Service at Bethesda, Md., was announced recently by Dr. Leonard Scheele, Surgeon General of the Public Health Service. One of the few radioisotope laboratories in America designed solely for medical research, the new Isotope Laboratory represents a major addition to already existing laboratory facilities at the National Institutes of Health.

* * *

Appointment of Dr. Sidney Olansky as Director of the Public Health Service's Venereal Disease Research Laboratory in Chamblee, Ga., was announced recently by Dr. Theodore J. Bauer, Chief of the Division of Venereal Disease.

A specialist in dermatology and syphilology, Dr. Olansky has been associated with the Public Health Service almost continuously since 1942. He spent two years as a resident in dermatology and syphilology at Duke University.

* * *

Some 100,000 children in the United States 10 years of age or less have undiscovered syphilis which they have had from birth, according to an article in the current issue of **The Child**, monthly periodical of the Children's Bureau, Federal Security Agency.

In an accompanying editorial in the same issue of **The Child**, Katherine F. Lenroot, Chief of the Children's Bureau, pointed out that the rate of acquired syphilis in the United States has been cut in half during the past four years, while the rate of congenital syphilis has remained almost constant.

DEPARTMENT OF DEFENSE

Clinical Practice in Medical Specialties Available in USAF Hospitals

Civilian physicians completing formal residency training may obtain additional clinical practice by obtaining Air Force reserve commissions and active duty with assignment to Air Force hospitals, Major General Harry G. Armstrong, the Surgeon General, announced recently.

Under this program civilian physicians who have completed formal residency training are given an opportunity to obtain clinical practice necessary to become certified in their specialties. The active duty tours, for one or more years, offered by the Air Force Medical Service make it possible for such physicians to complete the requirements of the various American medical specialty boards.

The specialties in which openings are available include internal medicine, general surgery, otorhinolaryngology (ear, nose and throat), obstetrics and gynecology, ophthalmology, anesthesiology, pediatrics, and psychiatry.

Detailed information and application forms for reserve appointments and tours of active duty for one or more years may be obtained upon written application to the Directorate of Staffing and Education, Office of the Surgeon General, Headquarters, U. S. Air Force, Washington 25, D C.

* * *

Tuberculosis Rate Among Navy Employees Drops 33 Per Cent in One Year

A 33 per cent decrease in the incidence of tuberculosis among Navy civilian employees has been reported by Rear Admiral C. A. Swanson, Surgeon General of the Navy, as a result of the Navy Medical Department's continuing chest x-ray program.

Reports from naval activities in the United States and overseas show that of a total of 213,442 civilian employees who were given x-ray examinations in 1949, four of every 1,000 employees had evidence of tuberculosis which required immediate treatment. In 1948, the incidence rate was six in every 1,000.

During each of the two years, three of every 1,000 Navy employees were found to have evidence of other chest diseases such as lung tumors and heart disease.

Under the Navy's tuberculosis control program, earlier and more effective treatment is provided for those affected than would be possible after noticeable symptoms had developed. Chest x-rays are made annually on all civilian employees, and at the time of their entering and leaving Naval employment.

Latin American surgeons and physicians will have an opportunity, most of them for the first time, to witness the latest demonstrations of surgical procedures by television during the coming summer months. The E. R. Squibb & Sons International Corporation is sponsoring a scientific project called "Video Medico" which it will put on in five of the more important countries in Latin America.

Easily the most ambitious project of its kind ever attempted, Squibb International will work in conjunction with International General Electric.

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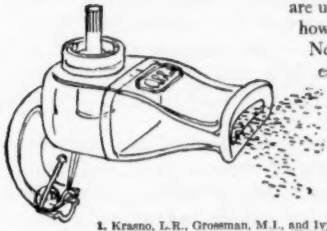

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1. Krasno, L.R., Grossman, M.I., and Ivy, A.C. (1949), The Inhalation of 1-(3',4'-Dihydroxyphenyl)-2-Isopropylaminoethanol (Norisodrine Sulfate Dust), J. Allergy, 20:111, March. 2. Krasno, L.R., Grossman, M., and Ivy, A.C. (1948), The Inhalation of Norisodrine Sulfate Dust, Science, 108:476, Oct. 29.

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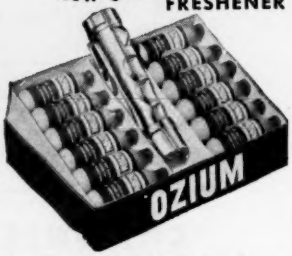

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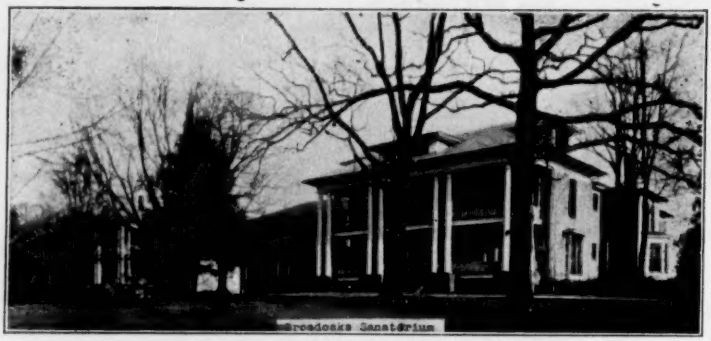

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*Perloff, W. H.: Am. J. Obst. & Gynec. 58:684 (Oct.) 1949.

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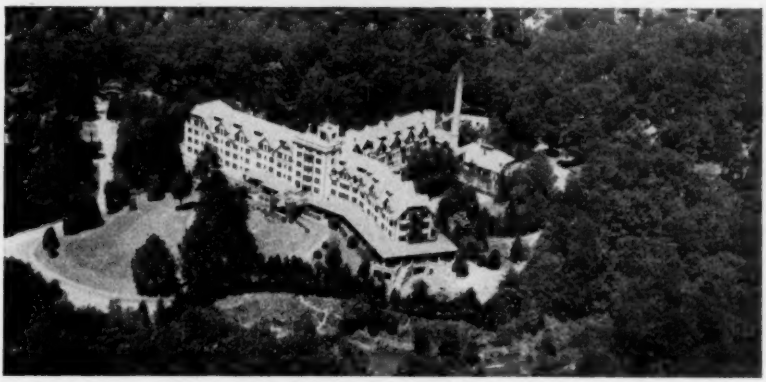

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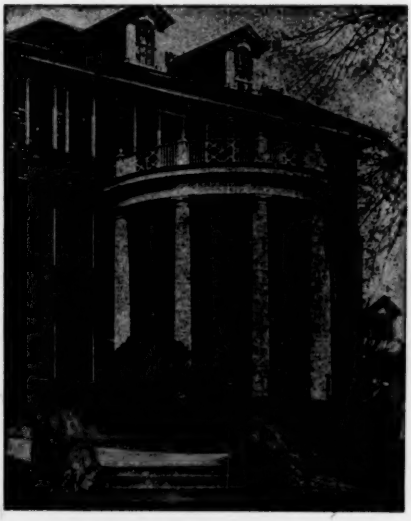

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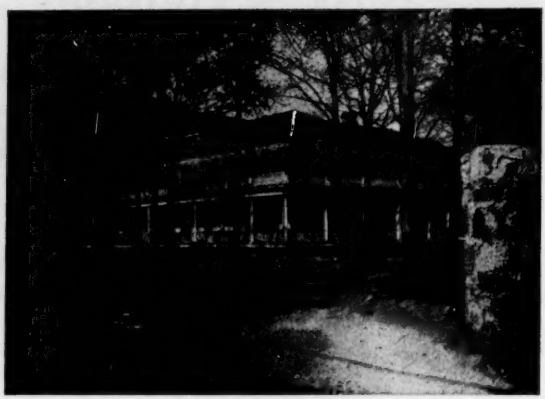

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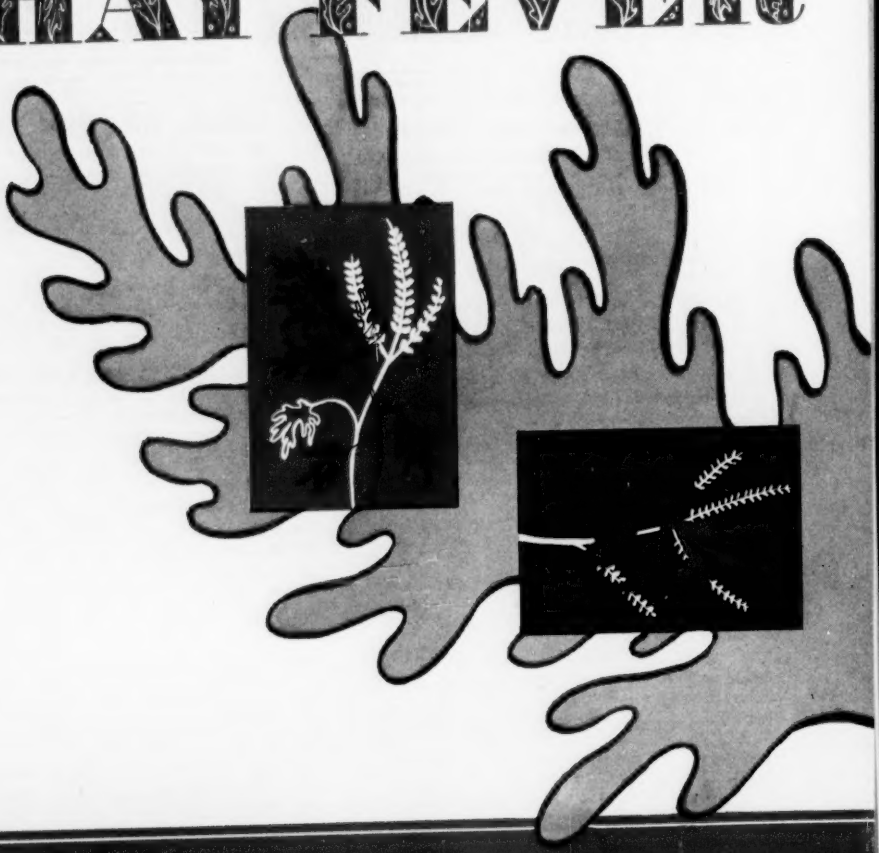

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